

FIG. 3

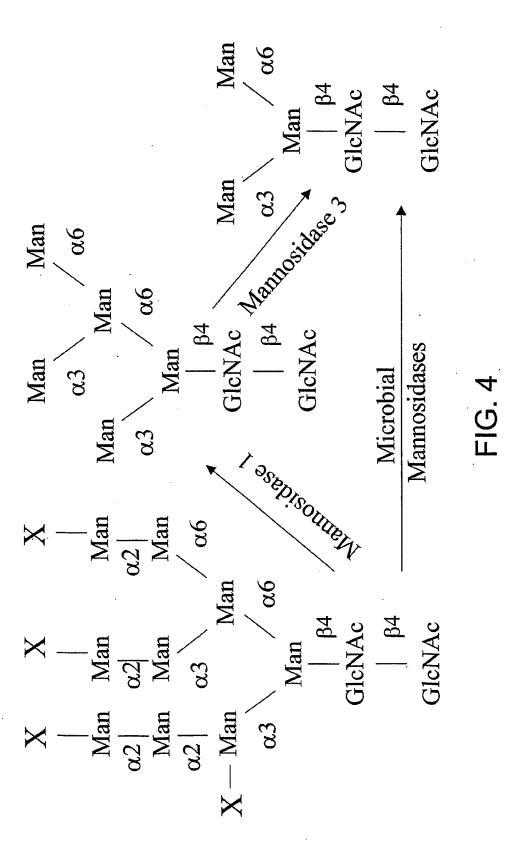
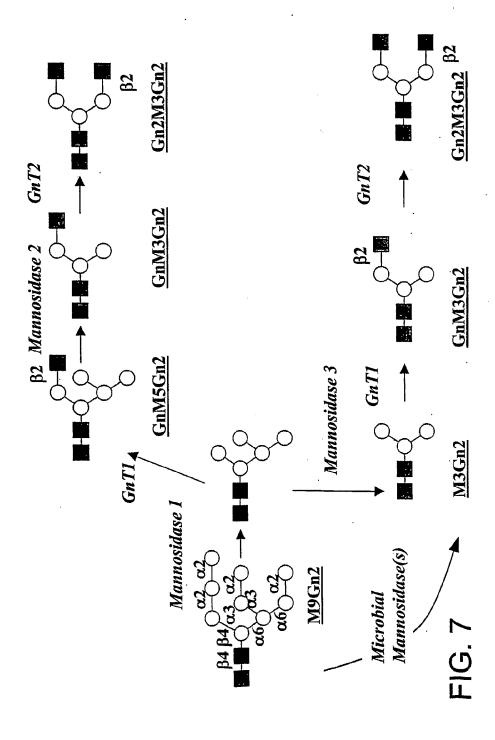
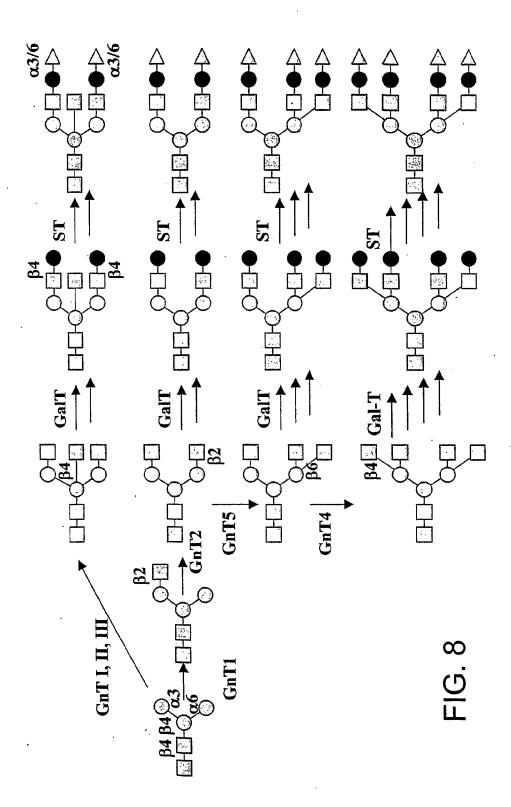


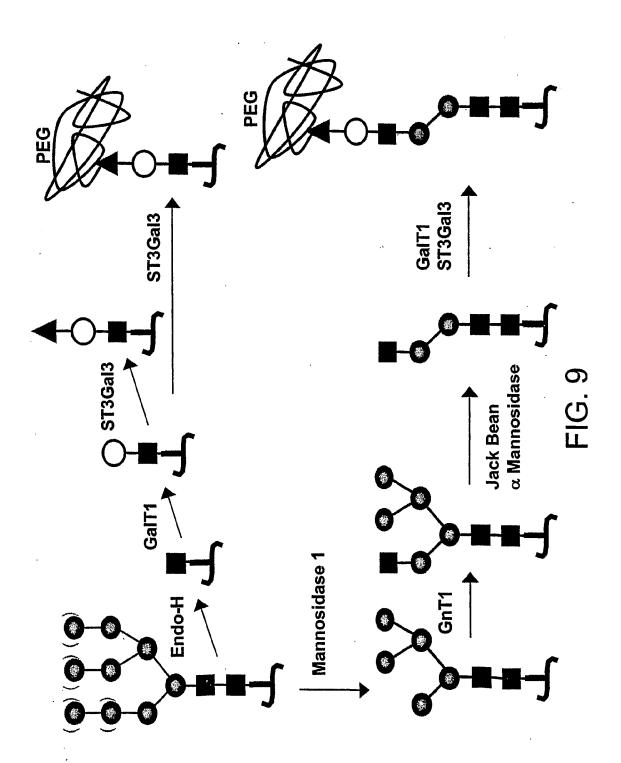
FIG. 6

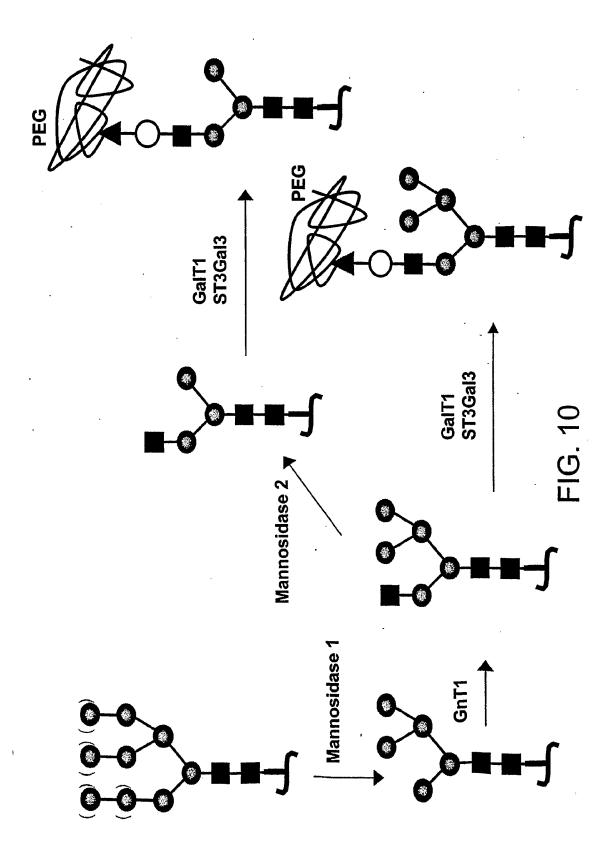


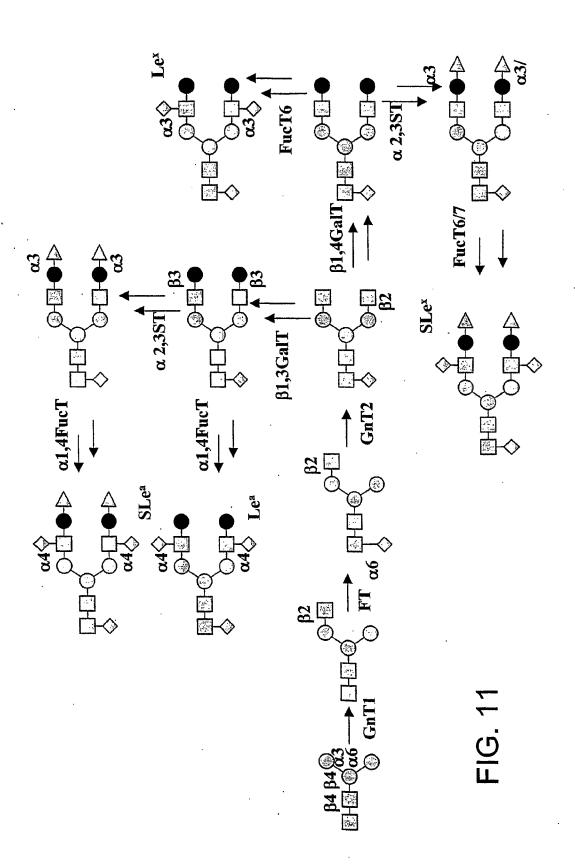
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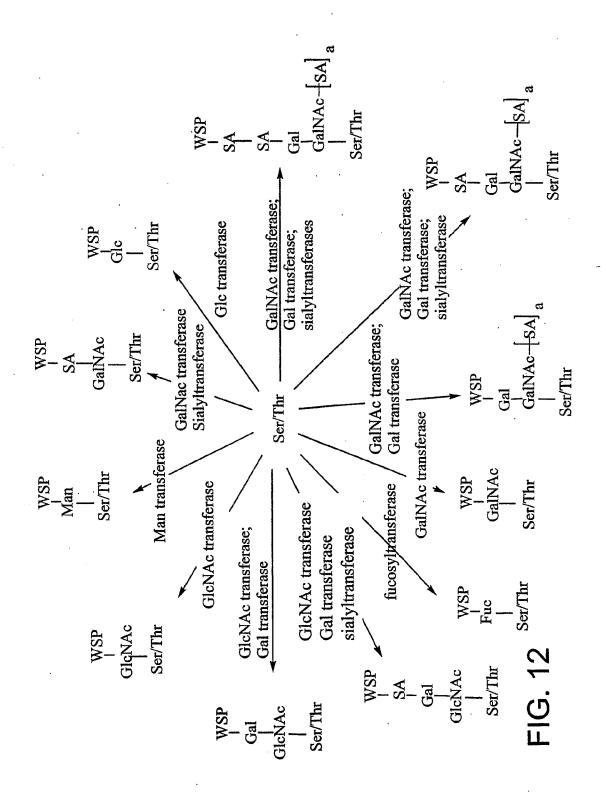
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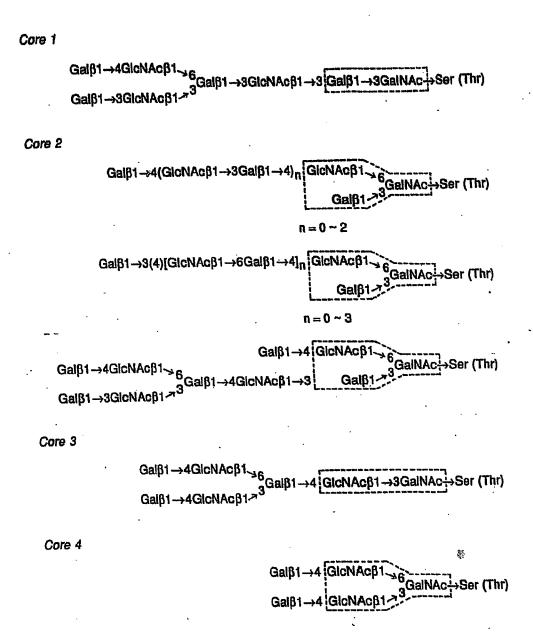
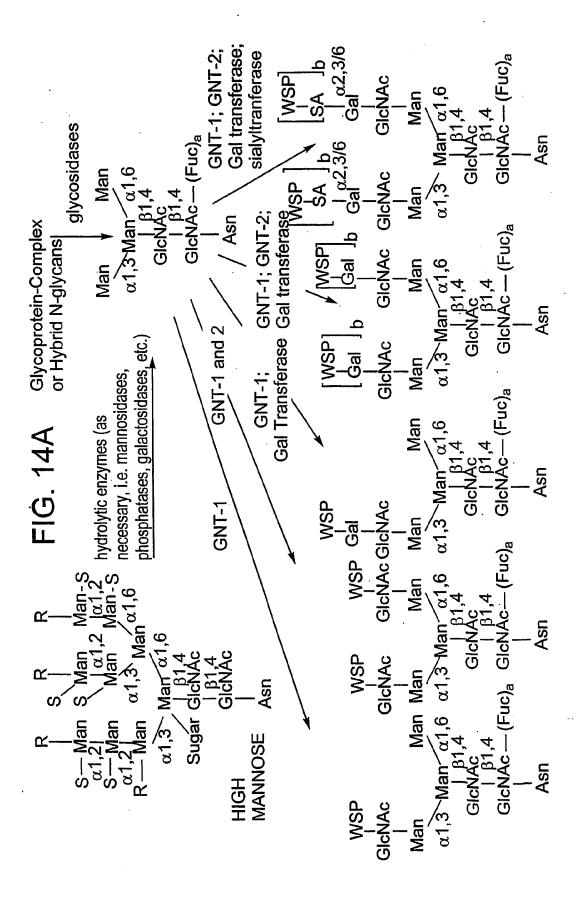
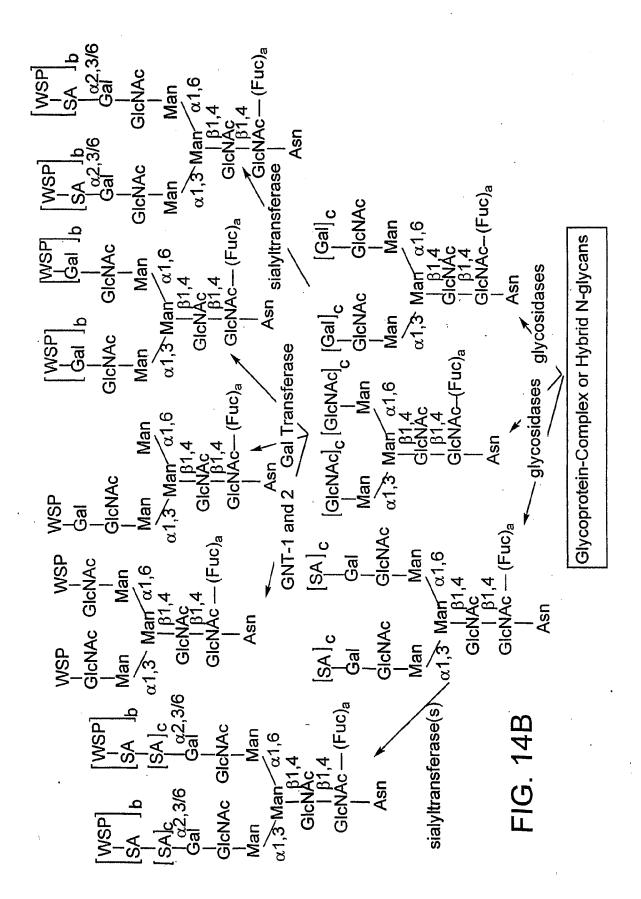


FIG. 13





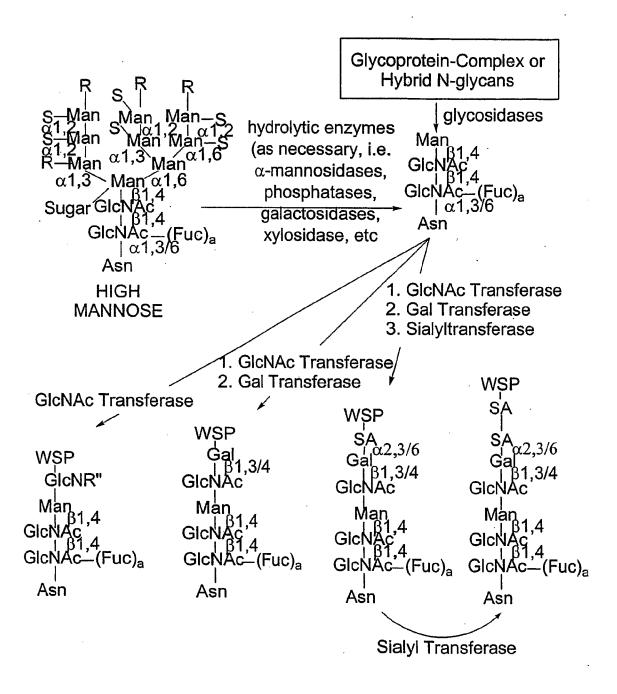


FIG. 15

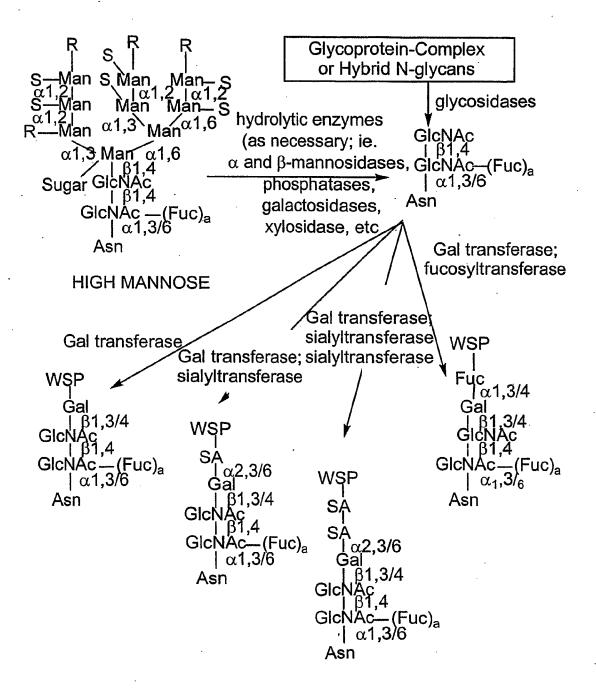


FIG. 16

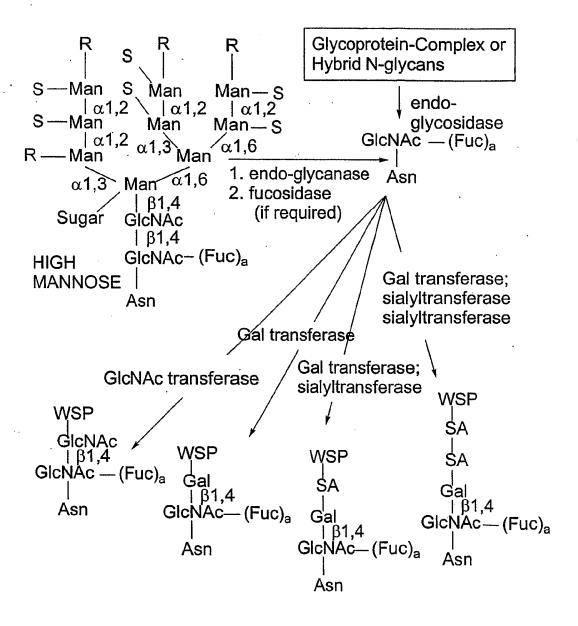
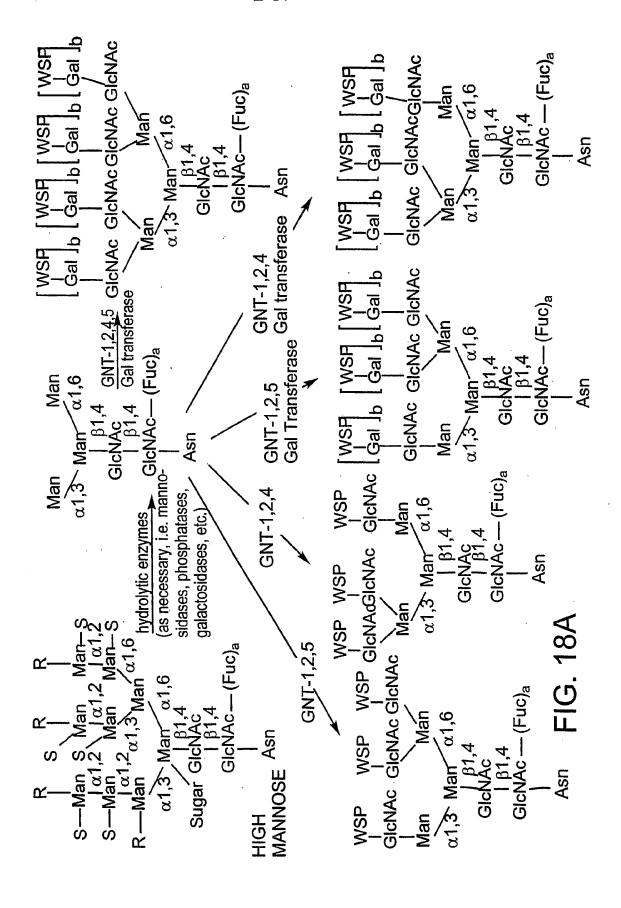
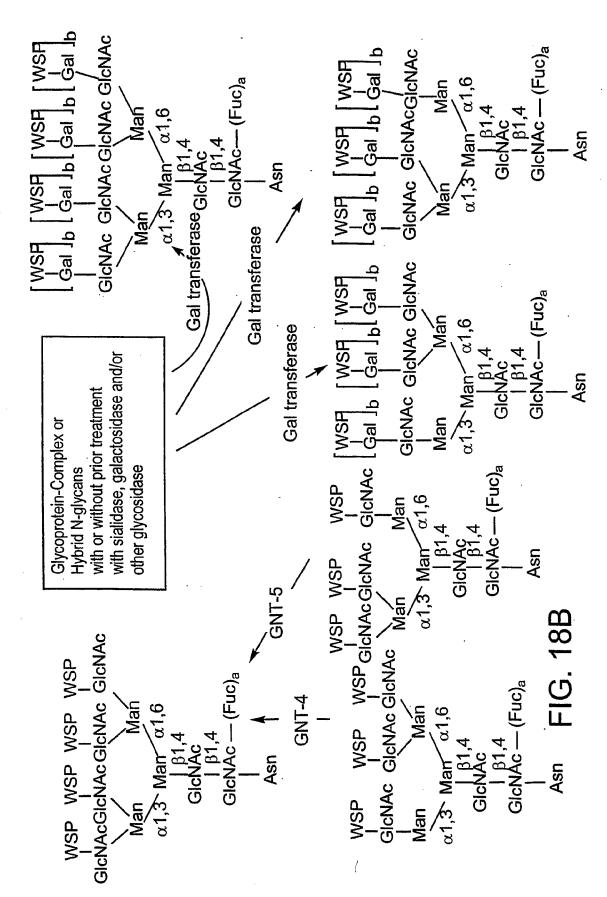
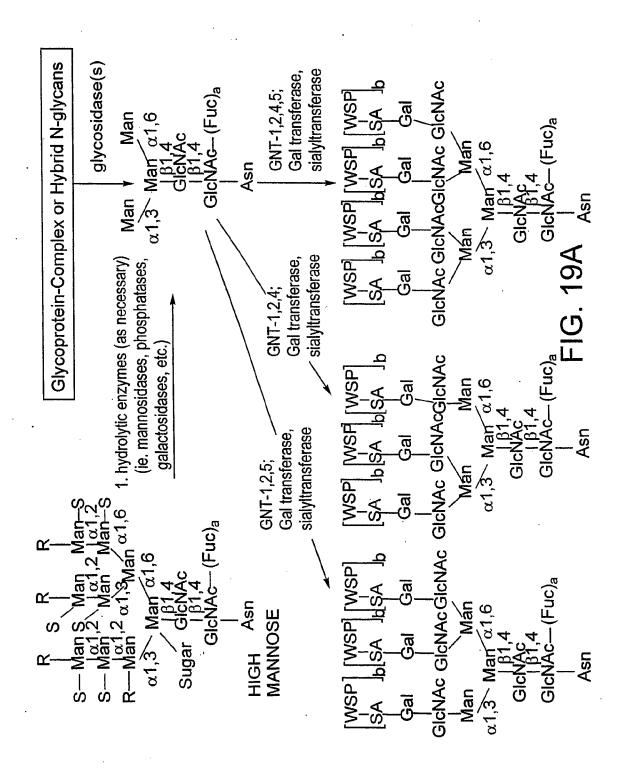
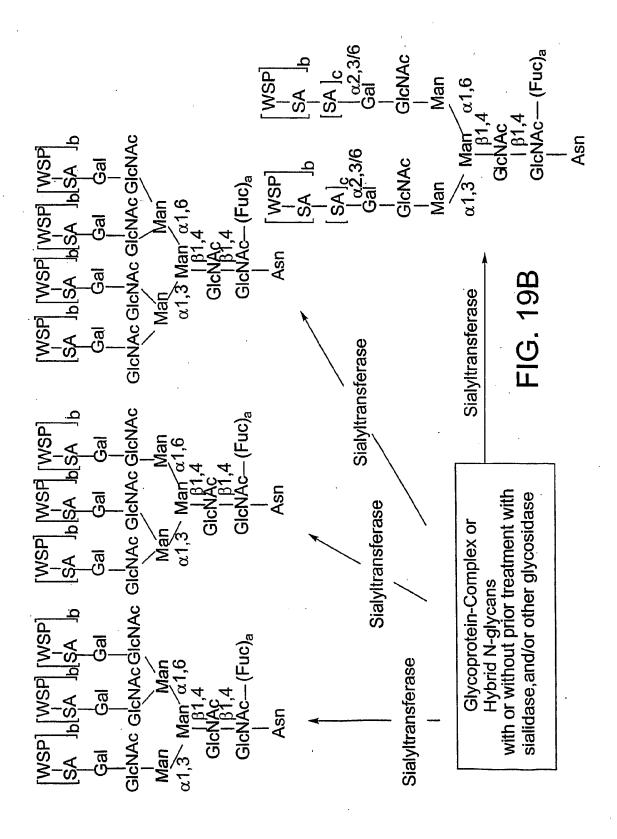


FIG. 17









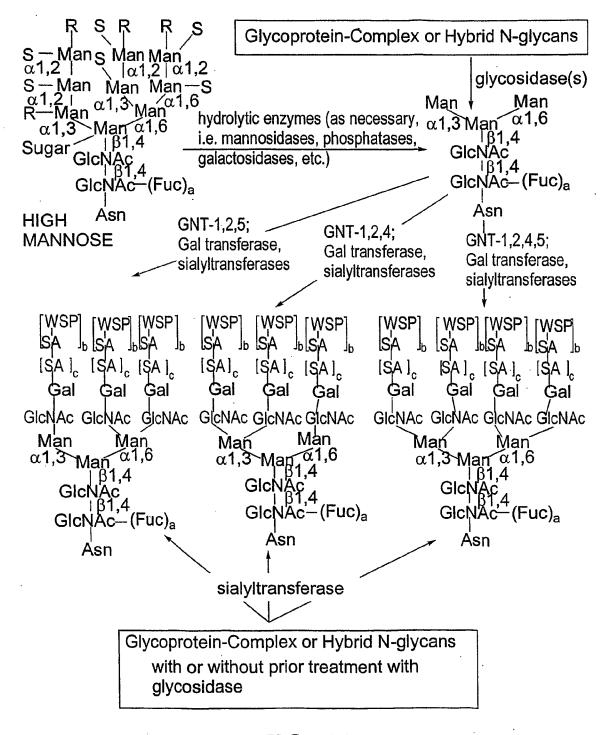
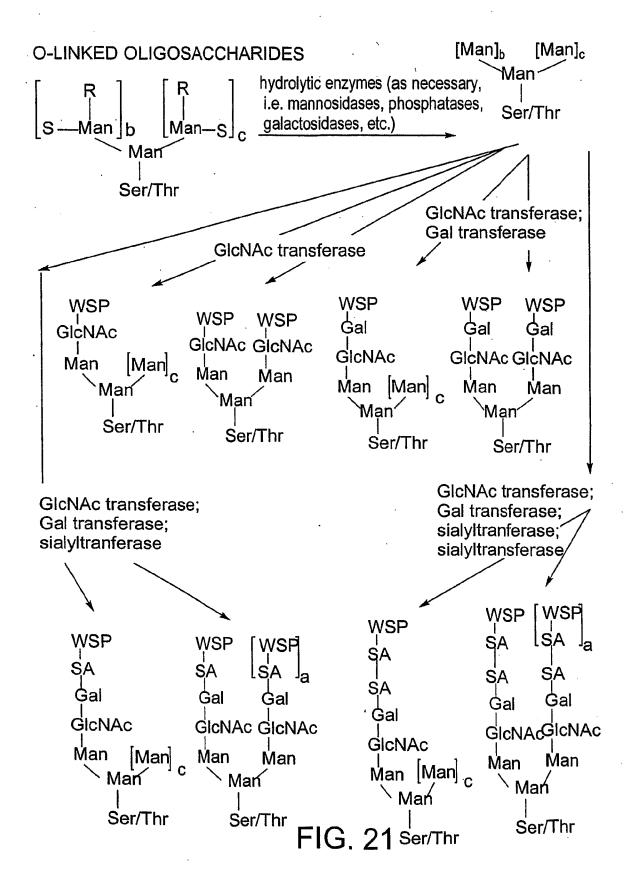
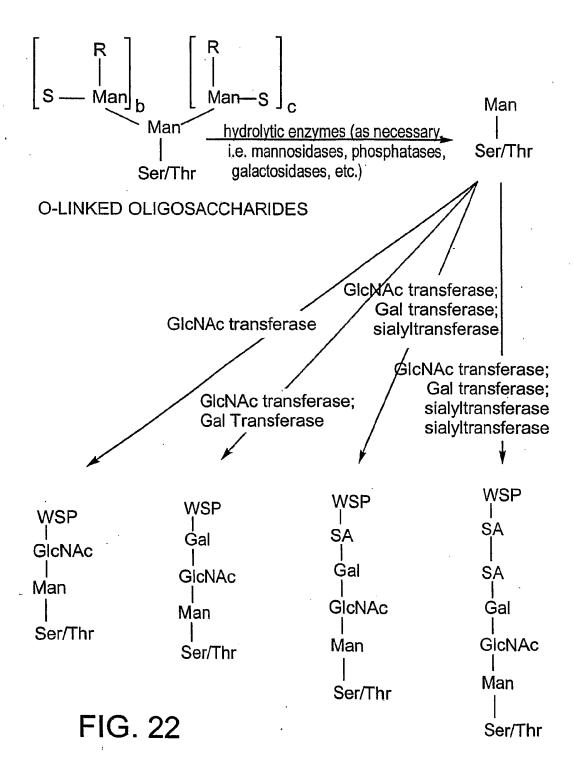
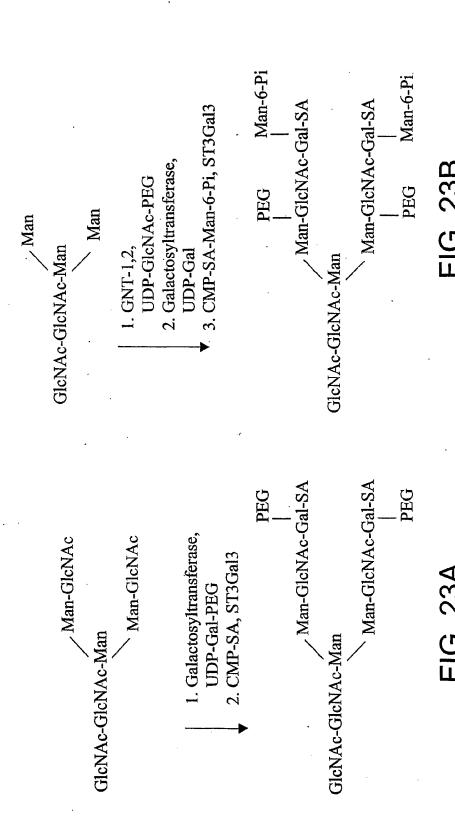
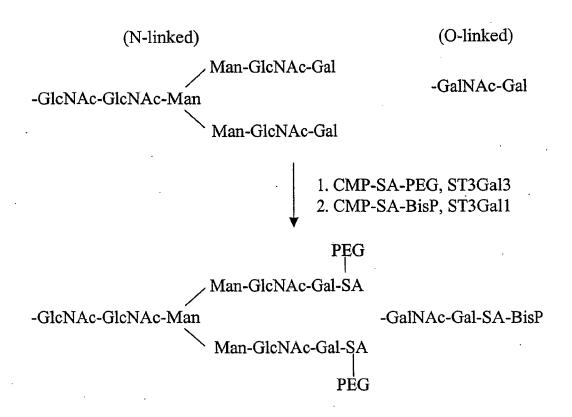


FIG. 20



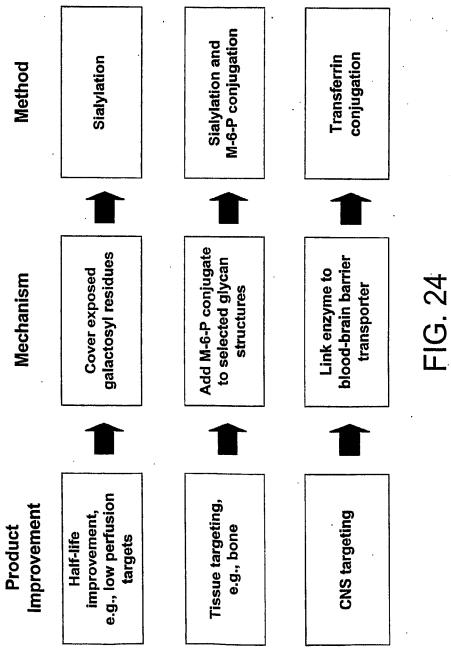


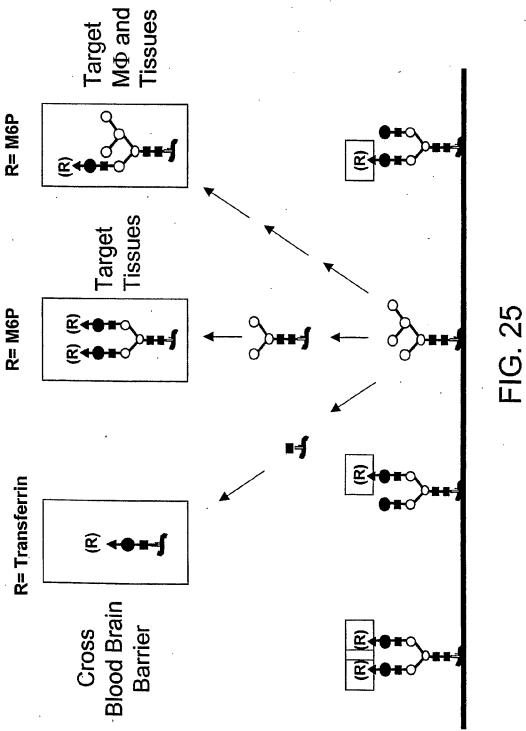


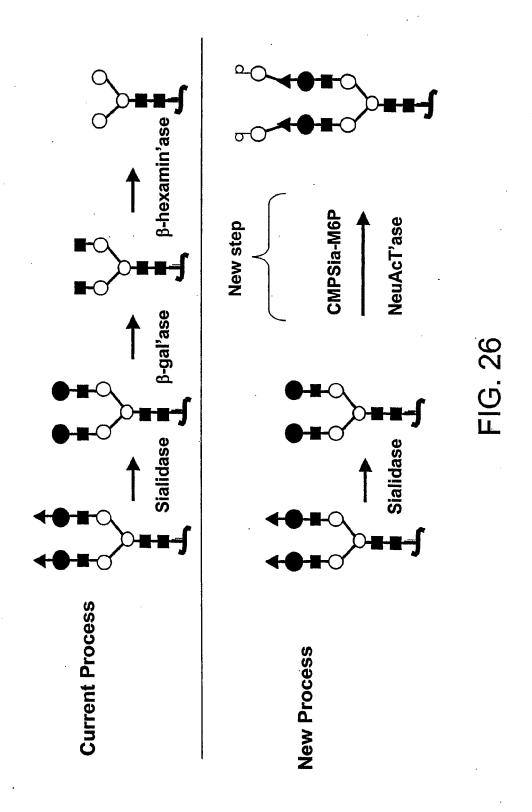


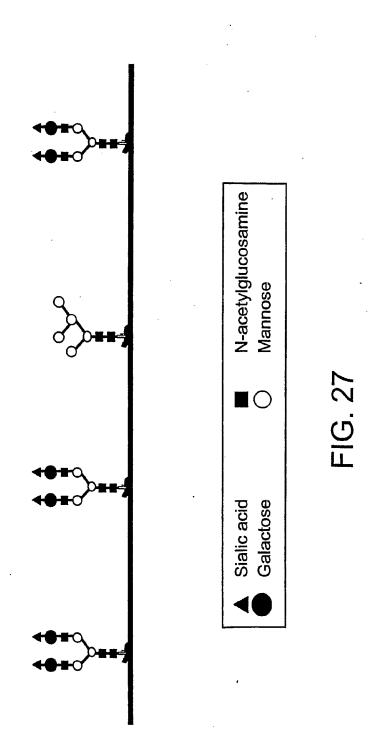
BisP =Linker-HN-CH(PO₃)₂

FIG. 23C









Al-201 - AutoImmune 12AP1/E5 -- Viventia Biotech AI-301 - AutoImmune 1964 -- Aventis AIDS vaccine - ANRS, CIBG, Hesed 20K growth hormone -- AMUR Biomed, Hollis-Eden, Rome, United 28P6/E6 -- Viventia Biotech Biomedical, American Home Products, 3-Hydroxyphthaloyl-beta-lactoglobulin -Maxygen 4-IBB ligand gene therapy airway receptor ligand -- IC Innovations 64-Cu MAb conjugate TETA-1A3 --AJvW 2 -- Aiinomoto Mallinckrodt Institute of Radiology AK 30 NGF -- Alkermes 64-Cu MAb conjugate TETA-cT84.66 Albuferon -- Human Genome Sciences 64-Cu Trastuzumab TETA conjugate albumin - Biogen, DSM Anti-Infectives, Genentech Genzyme Transgenics, PPL Therapeutics, A 200 -- Amgen TranXenoGen, Welfide Corp. A10255 – Eli Liliy aldesleukin -- Chiron A1PDX - Hedral Therapeutics alefacept -- Biogen A6 -- Angstrom Alemtuzumab aaAT-III -- Genzyme Allergy therapy -- ALK-Abello/Maxygen, Abciximab -- Centocor ALK-Abello/RP Scherer ABI.001 - Atlantic BioPharmaceuticals allergy vaccines -- Allergy Therapeutics ABT-828 - Abbott Alnidofibatide -- Aventis Pasteur Accutin Alnorine -- SRC VB VECTOR Actinohivin ALP 242 -- Gruenenthal activin -- Biotech Australia, Human Alpha antitrypsin -- Arriva/Hyland Therapeutics, Curis Immuno/ProMetic/Protease Sciences AD 439 – Tanox Alpha-1 antitrypsin – Cutter, Bayer, PPL AD 519 – Tanox Adalimumab -- Cambridge Antibody Tech. Therapeutics, Profile, ZymoGenetics, Arriva Adenocarcinoma vaccine – Biomira -- NIS Alpha-1 protease inhibitor -- Genzyme Adenosine deanimase -- Enzond Transgenics, Welfide Corp. Adenosine A2B receptor antagonists --Alpha-galactose fusion protein – Adenosine Therapeutics **Immunomedics** ADP-001 – Axis Genetics Alpha-galactosidase A -- Research AF 13948 – Affymax Corporation Technologies, Genzyme Afelimomab – Knoll Alpha-glucosidase - Genzyme, Novazyme AFP-SCAN - Immunomedics Alpha-lactalbumin AG 2195 – Corixa Alpha-L-iduronidase -- Transkaryotic agalsidase alfa -- Transkaryotic Therapies Therapies, BioMarin agalsidase beta -- Genzyme alteplase -- Genentech AGENT- Antisoma alvircept sudotox - NIH AI 300 - Autolmmune ALX-0600, a GLP-2 agonist -- NPS Allelix Al-101 - Teva Corp. Al-102 – Teva

FIG. 28A

Anti-alphavβ3 integrin MAb – Applied ALX1-11 -sNPS Pharmaceuticals Alzheimer's disease gene therapy Molecular Evolution Anti-angiogenesis monoclonal antibodies --AM-133 -- AMRAD KS Biomedix/Schering AG Amb a 1 immunostim conj. -- Dynavax Anti-B4 MAb-DC1 conjugate -- ImmunoGen AMD 3100 - AnorMED -- NIS Anti-B7 antibody PRIMATIZED -- IDEC AMD 3465 - AnorMED -- NIS AMD 3465 - AnorMED -- NIS Anti-B7-1 MAb 16-10A1 Anti-B7-1 MAb 1G10 AMD Fab -- Genentech Anti-B7-2 MAb GL-1 Amediplase – Menarini, Novartis Anti-B7-2-gelonin immunotoxin – AM-F9 Amoebiasis vaccine Antibacterials/antifungals --Diversa/IntraBiotics Amphiregulin -- Octagene Anti-beta-amyloid monoclonal antibodies -anakinra -- Amgen Cambridge Antibody Tech., Wyeth-Ayerst analgesic -- Nobex Anti-BLyS antibodies -- Cambridge ancestim -- Amgen Antibody Tech. /Human Genome Sciences AnergiX.RA – Corixa, Organon Antibody-drug conjugates -- Seattle Angiocidin -- InKine Genetics/Eos angiogenesis inhibitors -- ILEX Anti-C5 MAb BB5-1 -- Alexion AngioMab – Antisoma Angiopoietins -- Regeneron/Procter & Anti-C5 MAb N19-8 -- Alexion Anti-C8 MAb Gamble anticancer cytokines -- BioPulse angiostatin -- EntreMed Angiostatin/endostatin gene therapy -anticancer matrix - Telios Integra Anticancer monoclonal antibodies - ARIUS, Genetix Pharmaceuticals angiotensin-II, topical -- Maret Immunex anticancer peptides - Maxygen, Micrologix Anthrax -- EluSys Therapeutics/US Army Anticancer prodrug Tech. -- Alexion Medical Research Institute **Antibody Technologies** Anthrax vaccine Anti platelet-derived growth factor D human anticancer Troy-Bodies -- Affite -- Affitech monoclonal antibodies -- CuraGen anticancer vaccine -- NIH anticancers -- Epimmune Anti-17-1A MAb 3622W94 --Anti-CCR5/CXCR4 sheep MAb -- KS GlaxoSmithKline Biomedix Holdings Anti-2C4 MAb -- Genentech anti-4-1BB monoclonal antibodies -- Bristol- Anti-CD11a MAb KBA --Anti-CD11a MAb M17 Myers Squibb Anti-CD11a MAb TA-3 -Anti-Adhesion Platform Tech. -- Cytovax Anti-adipocyte MAb -- Cambridge Antibody Anti-CD11a MAb WT.1 --Anti-CD11b MAb -- Pharmacia Tech./ObeSys antiallergics -- Maxygen Anti-CD11b MAb LM2 Anti-CD154 MAb -- Biogen antiallergy vaccine -- Acambis Anti-CD16-anti-CD30 MAb -- Biotest Anti-alpha-4-integrin MAb

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Anti-CD4 MAb - Centocor, IDEC Anti-CD18 MAb -- Pharmacia Pharmaceuticals, Xenova Group Anti-CD19 MAb B43 -Anti-CD19 MAb -liposomal sodium butyrate Anti-CD4 MAb 16H5 Anti-CD4 MAb 4162W94 - GlaxoSmithKline conjugate -Anti-CD4 MAb B-F5 -- Diaclone Anti-CD147 Anti-CD4 MAb GK1-5 Anti-CD19 MAb-saporin conjugate -Anti-CD19-dsFv-PE38-immunotoxin -Anti-CD4 MAb KT6 Anti-CD4 MAb OX38 Anti-CD2 MAb 12-15 -Anti-CD4 MAb PAP conjugate -- Bristol-Anti-CD2 MAb B-E2 -- Diaclone Myers Squibb Anti-CD2 MAb OX34 -Anti-CD4 MAb RIB 5-2 Anti-CD2 MAb OX54 -Anti-CD4 MAb W3/25 Anti-CD2 MAb OX55 -Anti-CD4 MAb YTA 3.1.2 Anti-CD2 MAb RM2-1 Anti-CD4 MAb YTS 177-9 Anti-CD2 MAb RM2-2 Anti-CD40 ligand MAb 5c8 -- Biogen Anti-CD2 MAb RM2-4 Anti-CD40 MAb Anti-CD20 MAb BCA B20 Anti-CD20-anti-Fc alpha RI bispecific MAb -Anti-CD40 MAb 5D12 - Tanox Anti-CD44 MAb A3D8 Medarex, Tenovus Anti-CD44 MAb GKWA3 Anti-CD22 MAb-saporin-6 complex -Anti-CD44 MAb IM7 Anti-CD3 immunotoxin – Anti-CD44 MAb KM81 Anti-CD3 MAb 145-2C11 -- Pharming Anti-CD44 variant monoclonal antibodies --Anti-CD3 MAb CD4lgG conjugate --Corixa/Hebrew University Genentech Anti-CD3 MAb humanised - Protein Design, Anti-CD45 MAb BC8-I-131 Anti-CD45RB MAb RW Johnson Anti-CD48 MAb HuLy-m3 Anti-CD3 MAb WT32 Anti-CD48 MAb WM-63 Anti-CD3 MAb-ricin-chain-A conjugate – Anti-CD3 MAb-xanthine-oxidase conjugate Anti-CD5 MAb -- Becton Dickinson Anti-CD5 MAb OX19 Anti-CD30 MAb BerH2 -- Medac Anti-CD6 MAb Anti-CD7 MAb-PAP conjugate Anti-CD30 MAb-saporin conjugate Anti-CD7 MAb-ricin-chain-A conjugate Anti-CD30-scFv-ETA'-immunotoxin Anti-CD8 MAb – Amerimmune, Cytodyn, Anti-CD38 MAb AT13/5 Becton Dickinson Anti-CD38 MAb-saporin conjugate Anti-CD8 MAb 2-43 Anti-CD3-anti-CD19 bispecific MAb Anti-CD8 MAb OX8 Anti-CD3-anti-EGFR MAb Anti-CD80 MAb P16C10 -- IDEC Anti-CD3-anti-interleukin-2-receptor MAb Anti-CD3-anti-MOv18 MAb -- Centocor Anti-CD80 MAb P7C10 -- ID Vaccine Anti-CD8-idarubicin conjugate Anti-CD3-anti-SCLC bispecific MAb Anti-CEA MAb CE-25 Anti-CD4 idiotype vaccine Anti-CEA MAb MN 14 – Immunomedics

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Anti-heparanase human monocional Anti-CEA MAb MN14-PE40 conjugate – antibodies -- Oxford **Immunomedics** Glycosciences/Medarex Anti-CEA MAb T84.66-interleukin-2 Anti-hepatitis C virus human monoclonal conjugate antibodies -- XTL Biopharmaceuticals Anti-CEA sheep MAb -- KS Biomedix Anti-HER-2 antibody gene therapy Holdings Anti-herpes antibody -- Epicyte Anti-cell surface monoclonal antibodies --Anti-HIV antibody -- Epicyte Cambridge Antibody Tech. /Pharmacia anti-HIV catalytic antibody -- Hesed Biomed Anti-c-erbB2-anti-CD3 bifunctional MAb -anti-HIV fusion protein -- Idun Otsuka anti-HIV proteins -- Cangene Anti-CMV MAb -- Scotgen Anti-HM1-24 MAb -- Chugai Anti-complement Anti-hR3 MAb Anti-CTLA-4 MAb Anti-Human-Carcinoma-Antigen MAb --Anti-EGFR catalytic antibody -- Hesed **Epicyte** Biomed Anti-ICAM-1 MAb -- Boehringer Ingelheim anti-EGFR immunotoxin -- IVAX Anti-ICAM-1 MAb 1A-29 -- Pharmacia Anti-EGFR MAb -- Abgenix Anti-ICAM-1 MAb HA58 Anti-EGFR MAb 528 Anti-ICAM-1 MAb YN1/1.7.4 Anti-EGFR MAb KSB 107 -- KS Biomedix Anti-ICAM-3 MAb ICM3 -- ICOS Anti-EGFR MAb-DM1 conjugate --Anti-idiotype breast cancer vaccine 11D10 ImmunoGen Anti-idiotype breast cancer vaccine Anti-EGFR MAb-LA1 -ACA14C5 -Anti-EGFR sheep MAb -- KS Biomedix Anti-idiotype cancer vaccine -- ImClone Anti-FAP MAb F19-I-131 Systems/Merck KGaA ImClone, Viventia Anti-Fas IgM MAb CH11 Biotech Anti-Fas MAb Jo2 Anti-idiotype cancer vaccine 1A7 -- Titan Anti-Fas MAb RK-8 Anti-Flt-1 monoclonal antibodies -- ImClone Anti-idiotype cancer vaccine 3H1 -- Titan Anti-idiotype cancer vaccine TriAb -- Titan Anti-fungal peptides -- State University of Anti-idiotype Chlamydia trachomatis New York antifungal tripeptides -- BTG vaccine Anti-ganglioside GD2 antibody-interleukin-2 Anti-idiotype colorectal cancer vaccine --Novartis fusion protein -- Lexigen Anti-idiotype colorectal cancer vaccine --Anti-GM2 MAb -- Kyowa Anti-GM-CSF receptor monoclonal Onyvax Anti-idiotype melanoma vaccine -- IDEC antibodies -- AMRAD **Pharmaceuticals** Anti-gp130 MAb -- Tosoh Anti-idiotype ovarian cancer vaccine ACA Anti-HCA monoclonal antibodies --125 AltaRex/Epigen Anti-idiotype ovarian cancer vaccine AR54 -Anti-hCG antibodies -- Abgenix/AVI - AltaRex BioPharma

Anti-L-selectin monoclonal antibodies --Anti-idiotype ovarian cancer vaccine CA-Protein Design Labs, Abgenix, Stanford 125 - AltaRex, Biomira Anti-IgE catalytic antibody -- Hesed Biomed University Anti-MBL monoclonal antibodies --Anti-IgE MAb E26 -- Genentech Alexion/Brigham and Women's Hospital Anti-IGF-1 MAb Anti-MHC monoclonal antibodies anti-inflammatory -- GeneMax Anti-MIF antibody humanised – IDEC, anti-inflammatory peptide -- BTG Cytokine PharmaSciences anti-integrin peptides -- Burnha Anti-interferon-alpha-receptor MAb 64G12 - Anti-MRSA/VRSA sheep MAb -- KS Biomedix Holdings Pharma Pacific Management Anti-mu MAb -- Novartis Anti-interferon-gamma MAb -- Protein Anti-MUC-1 MAb Design Labs Anti-interferon-gamma polyclonal antibody - Anti-MUC 18 Anti-Nogo-A MAb IN1 - Advanced Biotherapy Anti-nuclear autoantibodies -- Procyon Anti-interleukin-10 MAb -Anti-ovarian cancer monoclonal antibodies -Anti-interleukin-12 MAb -Anti-interleukin-1-beta polyclonal antibody -- - Dompe Anti-p185 monoclonal antibodies R&D Systems Anti-p43 MAb Anti-interleukin-2 receptor MAb 2A3 Antiparasitic vaccines Anti-interleukin-2 receptor MAb 33B3-1 --Anti-PDGF/bFGF sheep MAb -- KS Immunotech Biomedix Anti-interleukin-2 receptor MAb ART-18 Anti-properdin monoclonal antibodies --Anti-interleukin-2 receptor MAb LO-Tact-1 Abgenix/Gliatech Anti-interleukin-2 receptor MAb Mikbeta1 Anti-PSMA (prostrate specific membrane Anti-interleukin-2 receptor MAb NDS61 antigen) Anti-interleukin-4 MAb 11B11 Anti-PSMA MAb J591 -- BZL Biologics Anti-interleukin-5 MAb -- Wallace Anti-Rev MAb gene therapy -Laboratories Anti-RSV antibodies - Epicyte, Intracell Anti-interleukin-6 MAb – Centocor, Anti-RSV monoclonal antibodies --Diaclone, Pharmadigm Medarex/Medimmune, Applied Molecular Anti-interleukin-8 MAb -- Abgenix Evolution/Medimmune Anti-interleukin-8 MAb - Xenotech Anti-RSV MAb, inhalation --Anti-JL1 MAb Anti-Klebsiella sheep MAb -- KS Biomedix Alkermes/Medimmune Anti-RT gene therapy **Holdings** Antisense K-ras RNA gene therapy Anti-Laminin receptor MAb-liposomal Anti-SF-25 MAb doxorubicin conjugate Anti-sperm antibody -- Epicyte Anti-LCG MAb -- Cytoclonal Anti-Tac(Fv)-PE38 conjugate Anti-lipopolysaccharide MAb -- VitaResc Anti-TAPA/CD81 MAb AMP1 Anti-tat gene therapy

Anti-TCR-alphabeta MAb H57-597 Anti-TCR-alphabeta MAb R73 Anti-tenascin MAb BC-4-I-131 Anti-TGF-beta human monoclonal antibodies -- Cambridge Antibody Tech., Genzyme Anti-TGF-beta MAb 2G7 -- Genentech Antithrombin III -- Genzyme Transgenics, Aventis, Bayer, Behringwerke, CSL, Myriad Anti-Thy1 MAb Anti-Thy1.1 MAb Anti-tissue factor/factor VIIA sheep MAb --KS Biomedix Anti-TNF monoclonal antibodies -Centocor, Chiron, Peptech, Pharacia, Anti-TNF sheep MAb -- KS Biomedix Holdings Anti-TNFalpha MAb -- Genzyme Anti-TNFalpha MAb B-C7 -- Diaclone Anti-tooth decay MAb -- Planet BioTech. Anti-TRAIL receptor-1 MAb -- Takeda Antitumour RNases -- NIH Anti-VCAM MAb 2A2 -- Alexion Anti-VCAM MAb 3F4 -- Alexion Anti-VCAM-1 MAb Anti-VEC MAb -- ImClone Anti-VEGF MAb -- Genentech Anti-VEGF MAb 2C3 Anti-VEGF sheep MAb -- KS Biomedix Holdings Anti-VLA-4 MAb HP1/2 -- Biogen Anti-VLA-4 MAb PS/2 Anti-VLA-4 MAb R1-2 Anti-VLA-4 MAb TA-2 Anti-VAP-1 human MAb Anti-VRE sheep MAb -- KS Biomedix Holdings ANUP -- TranXenoGen ANUP-1 -- Pharis

AOP-RANTES -- Senetek Apan-CH -- Praecis Pharmaceuticals APC-8024 -- Demegen ApoA-1 -- Milano, Pharmacia Apogen -- Alexion apolipoprotein A1 -- Avanir Apolipoprotein E -- Bio-Tech. General Applaggin -- Biogen aprotinin -- ProdiGene APT-070C -- AdProTech AR 177 -- Aronex Pharmaceuticals AR 209 -- Aronex Pharmaceuticals, Antigenics AR545C ARGENT gene delivery systems -- ARIAD Arresten ART-123 -- Asahi Kasei arylsulfatase B -- BioMarin Arylsulfatase B, Recombinant human --BioMarin AS 1051 -- Ajinomoto ASI-BCL -- Intracell Asparaginase - Merck ATL-101 -- Alizyme Atrial natriuretic peptide -- Pharis Aurintricarboxylic acid-high molecular weight Autoimmune disorders -- GPC Biotech/MorphoSys Autoimmune disorders and transplant rejection -- Bristol-Myers Squibb/Genzyme Tra Autoimmune disorders/cancer --Abgenix/Chiron, CuraGen Autotaxin -Avicidin -- NeoRx axogenesis factor-1 -- Boston Life Sciences Axokine -- Regeneron B cell lymphoma vaccine -- Biomira B7-1 gene therapy -BABS proteins -- Chiron

FIG. 28F

BMP 2 -- Genetics Institute/Medtronic-BAM-002 -- Novelos Therapeutics Sofamor Danek, Genetics Institute/ Basiliximab (anti CD25 MAb) -- Novartis Collagenesis, Genetics Bay-16-9996 -- Bayer Institute/Yamanouch Bay-39-9437 -- Bayer BMP 2 gene therapy Bay-50-4798 -- Bayer BMP 52 -- Aventis Pasteur, Biopharm BB-10153 -- British Biotech BMP-2 -- Genetics Institute BBT-001 -- Bolder BioTech. BMS 182248 -- Bristol-Myers Squibb BBT-002 -- Bolder BioTech. BMS 202448 -- Bristol-Myers Squibb BBT-003 -- Bolder BioTech. bone growth factors -- IsoTis BBT-004 -- Bolder BioTech. BPC-15 -- Pfizer BBT-005 -- Bolder BioTech. brain natriuretic peptide -BBT-006 -- Bolder BioTech. Breast cancer -- Oxford BBT-007 -- Bolder BioTech. GlycoSciences/Medarex BCH-2763 -- Shire Breast cancer vaccine -- Therion Biologics, BCSF -- Millenium Biologix Oregon BDNF -- Regeneron - Amgen Becaplermin -- Johnson & Johnson, Chiron BSSL -- PPL Therapeutics BST-2001 – BioStratum Bectumomab - Immunomedics BST-3002 -- BioStratum Beriplast -- Aventis Beta-adrenergic receptor gene therapy --BTI 322 butyrylcholinesterase -- Shire University of Arkansas C 6822 -- COR Therapeutics bFGF -- Scios C1 esterase inhibitor -- Pharming BI 51013 -- Behringwerke AG C3d adjuvant -- AdProTech BIBH 1 -- Boehringer Ingelheim BIM-23190 -- Beaufour-Ipsen CAB-2.1 -- Millennium calcitonin - Inhale Therapeutics Systems, birch pollen immunotherapy -- Pharmacia Aventis, Genetronics, TranXenoGen, bispecific fusion proteins -- NIH Unigene, Rhone Poulenc Rohrer Bispecific MAb 2B1 -- Chiron calcitonin -- oral - Nobex, Emisphere, Bitistatin Pharmaceutical Discovery BIWA 4 -- Boehringer Ingelheim Calcitonin gene-related peptide -- Asahi blood substitute – Northfield, Baxter Intl. Kasei -- Unigene BLP-25 -- Biomira BLS-0597 -- Boston Life Sciences calcitonin, human -- Suntory calcitonin, nasal – Novartis, Unigene BLyS -- Human Genome Sciences calcitonin, Panoderm -- Elan BLyS radiolabelled -- Human Genome calcitonin, Peptitrol -- Shire Sciences calcitonin, salmon -- Therapicon BM 06021 -- Boehringer Mannheim calin -- Biopharm BM-202 -- BioMarin Calphobindin I BM-301 -- BioMarin calphobindin I -- Kowa BM-301 -- BioMarin calreticulin -- NYU BM-302 -- BioMarin

CD4 fusion toxin -- Senetek Campath-1G CD4 IgG -- Genentech Campath-1M CD4 receptor antagonists -cancer therapy -- Cangene Pharmacopeia/Progenics cancer vaccine - Aixlie, Aventis Pasteur, CD4 soluble -- Progenics Center of Molecular Immunology, YM CD4, soluble -- Genzyme Transgenics BioSciences, Cytos, Genzyme, CD40 ligand -- Immunex Transgenics, Globelmmune, Igeneon, CD4-ricin chain A -- Genentech ImClone, Virogenetics, InterCell, Iomai, CD59 gene therapy -- Alexion Jenner Biotherapies, Memorial Sloan-Kettering Cancer Center, Sydney Kimmel CD8 TIL cell therapy -- Aventis Pasteur CD8. soluble -- Avidex Cancer Center, Novavax, Protein CD95 ligand -- Roche Sciences, Argonex, SIGA CDP 571 -- Celltech Cancer vaccine ALVAC-CEA B7.1 --Aventis Pasteur/Therion Biologics CDP 850 -- Celltech CDP-860 (PEG-PDGF MAb) -- Celltech Cancer vaccine CEA-TRICOM -- Aventis CDP 870 -- Celltech Pasteur/Therion Biologics CDS-1 -- Ernest Orlando Cancer vaccine gene therapy -- Cantab Cedelizumab -- Ortho-McNeil **Pharmaceuticals** Cetermin -- Insmed Cancer vaccine HER-2/neu -- Corixa Cancer vaccine THERATOPE -- Biomira CETP vaccine -- Avant cancer vaccine, PolyMASC -- Valentis Cetrorelix Cetuximab Candida vaccine – Corixa, Inhibitex CGH 400 -- Novartis Canstatin -- ILEX CGP 42934 -- Novartis CAP-18 -- Panorama CGP 51901 – Tanox Cardiovascular gene therapy -- Collateral CGRP -- Unigene **Therapeutics CGS 27913 -- Novartis** carperitide -- Suntory CGS 32359 -- Novartis Casocidin-1 -- Pharis Chagas disease vaccine -- Corixa CAT 152 -- Cambridge Antibody Tech. CAT 192 -- Cambridge Antibody Tech. chemokines -- Immune Response CHH 380 -- Novartis CAT 213 -- Cambridge Antibody Tech. chitinase - Genzyme, ICOS Catalase-- Enzon Chlamydia pneumoniae vaccine -- Antex Cat-PAD -- Circassia **Biologics** CB 0006 -- Celltech Chlamydia trachomatis vaccine -- Antex CCK(27-32)-- Akzo Nobel **Biologics** CCR2-641 -- NIH Chlamydia vaccine -- GlaxoSmithKline CD. Procept -- Paligent Cholera vaccine CVD 103-HgR -- Swiss CD154 gene therapy Serum and Vaccine Institute Berne CD39 -- Immunex Cholera vaccine CVD 112 -- Swiss Serum CD39-L2 -- Hyseq and Vaccine Institute Berne CD39-L4 -- Hyseq

Cholera vaccine inactivated oral -- SBL CRL 1605 -- CytRx CS-560 -- Sankyo Vaccin CSF -- ZymoGenetics Chrysalin -- Chrysalis BioTech. CSF-G - Hangzhou, Dong-A, Hanmi CI-782 -- Hitachi Kase CSF-GM - Cangene, Hunan, LG Chem Ciliary neurotrophic factor – Fidia, Roche CSF-M -- Zarix CIM project -- Active Biotech CT 1579 - Merck Frosst CL 329753 -- Wyeth-Ayerst CT 1786 - Merck Frosst CL22, Cobra -- ML Laboratories CT-112[^] -- BTG Clenoliximab -- IDEC CTB-134L -- Xenova Clostridium difficile antibodies -- Epicyte CTC-111 -- Kaketsuken clotting factors -- Octagene CTGF -- FibroGen CMB 401 -- Celltech CTLA4-Ig -- Bristol-Myers Squibb CNTF -- Sigma-Tau CTLA4-Ig gene therapy – Cocaine abuse vaccine – Cantab, CTP-37 -- AVI BioPharma ImmuLogic, Scripps C-type natriuretic peptide -- Suntory coccidiomycosis vaccine -- Arizo CVS 995 - Corvas Intl. collagen -- Type I -- Pharming Collagen formation inhibitors -- FibroGen CX 397 – Nikko Kyodo Collagen/hydroxyapatite/bone growth factor CY 1747 -- Epimmune -- Aventis Pasteur, Biopharm, Orquest CY 1748 -- Epimmune Cyanovirin-N collagenase -- BioSpecifics Colorectal cancer vaccine -- Wistar Institute Cystic fibrosis therapy -- CBR/IVAX Component B, Recombinant -- Serono CYT 351 Connective tissue growth factor inhibitors -- cytokine Traps -- Regeneron cytokines - Enzon, Cytoclonal FibroGen/Taisho Cytomegalovirus glycoprotein vaccine -Contortrostatin Chiron, Aquila Biopharmaceuticals, contraceptive vaccine -- Zonagen Contraceptive vaccine hCG Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live -- Aventis Contraceptive vaccine male reversible --Pasteur **IMMUCON** Cytosine deaminase gene therapy --Contraceptive vaccine zona pellucida --GlaxoSmithKline Zonagen Copper-64 labelled MAb TETA-1A3 -- NCI DA-3003 -- Dong-A DAB389interleukin-6 -- Senetek Coralyne DAB389interleukin-7 Corsevin M DAC:GLP-2 -- ConjuChem, Inc. C-peptide analogues -- Schwarz Daclizumab (anti-IL2R MAb) - Protein CPI-1500 -- Consensus Design Labs CRF -- Neurobiological Tech. DAMP[^] -- Incyte Genomics cRGDfV pentapeptide -Daniplestim -- Pharmacia CRL 1095 -- CytRx darbepoetin alfa -- Amgen CRL 1336 -- CytRx

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dural graft matrix -- Integra DBI-3019 -- Diabetogen Duteplase – Baxter Intl. DCC -- Genzyme DWP-401 -- Daewoong DDF -- Hyseq DWP-404 -- Daewoong decorin - Integra, Telios DWP-408 -- Daewoong defensins -- Large Scale Biology Dx 88 (Epi-KAL2) -- Dyax **DEGR-VIIa** Dx 890 (elastin inhibitors) -- Dyax Delmmunised antibody 3B6/22 AGEN E coli O157 vaccine -- NIH Deimmunised anti-cancer antibodies --E21-R -- BresaGen Biovation/Viragen Eastern equine encephalitis virus vaccine – Dendroamide A Dengue vaccine -- Bavarian Nordic, Merck Echicetin --Echinhibin 1 – denileukin diftitox -- Ligand Echistatin -- Merck **DES-1101 -- Desmos** Echitamine desirudin -- Novartis Ecromeximab – Kyowa Hakko desmopressin -- Unigene Desmoteplase - Merck, Schering AG EC-SOD -- PPL Therapeutics Eculizumab (5G1.1) -- Alexion Destabilase Diabetes gene therapy - DeveloGen, Pfizer EDF -- Ajinomoto EDN derivative -- NIH Diabetes therapy -- Crucell Diabetes type 1 vaccine -- Diamyd EDNA -- NIH Edobacomab -- XOMA **Therapeutics** Edrecolomab -- Centocor DiaCIM -- YM BioSciences EF 5077 dialytic oligopeptides -- Research Corp Efalizumab -- Genentech Diamyd -- Diamyd Therapeutics EGF fusion toxin - Seragen, Ligand DiaPep227-- Pepgen EGF-P64k vaccine -- Center of Molecular DiavaX -- Corixa **Immunology** Digoxin MAb -- Glaxo Diphtheria tetanus pertussis-hepatitis B EL 246 -- LigoCyte elastase inhibitor -- Synergen vaccine -- GlaxoSmithKline elcatonin -- Therapicon DIR therapy -- Solis Therapeutics -EMD 72000 -- Merck KGaA DNase -- Genentech Emdogain -- BIORA Dornase alfa -- Genentech emfilermin -- AMRAD Dornase alfa, inhalation -- Genentech Emoctakin -- Novartis Doxorubicin-anti-CEA MAb conjugate enamel matrix protein -- BIORA **Immunomedics** Endo III -- NYU DP-107 -- Trimeris endostatin - EntreMed, Pharis drotrecogin alfa -- Eli Lilly Enhancins -- Micrologix DTctGMCSF Enlimomab -- Isis Pharm. DTP-polio vaccine -- Aventis Pasteur Enoxaparin sodium -- Pharmuka DU 257-KM231 antibody conjugate --

Kyowa

enzyme linked antibody nutrient depletion therapy -- KS Biomedix Holdings Eosinophil-derived neutralizing agent -EP-51216 -- Asta Medica EP-51389 -- Asta Medica EPH family ligands -- Regeneron Epidermal growth factor -- Hitachi Kasei, Johnson & Johnson Epidermal growth factor fusion toxin --Senetek Epidermal growth factor-genistein – EPI-HNE-4 -- Dyax EPI-KAL2 -- Dyax Epoetin-alfa – Amgen, Dragon Pharmaceuticals, Nanjing Huaxin Epratuzumab – Immunomedics Epstein-Barr virus vaccine --Aviron/SmithKline Beecham, Bioresearch Eptacog alfa -- Novo Nordisk Eptifibatide -- COR Therapeutics erb-38 -Erlizumab -- Genentech erythropoietin -- Alkermes, ProLease, Dong-Fas (delta) TM protein -- LXR BioTech. A, Elanex, Genetics Institute, LG Chem, Protein Sciences, Serono, Snow Brand, SRC VB VECTOR, Transkaryotic **Therapies** Erythropoietin Beta -- Hoffman La Roche Erythropoietin/Epoetin alfa -- Chugai Escherichia coli vaccine -- North American Vaccine, SBL Vaccin, Swiss Serum and Vaccine Institute Berne etanercept - Immunex examorelin – Mediolanum

Exendin 4 -- Amylin

exonuclease VII

F-992 -- Fornix

F 105 - Centocor

Factor IX -- Alpha Therapeutics, Welfide

Corp., CSL, enetics Institute/AHP,

Pharmacia, PPL Therapeutics

Factor IX gene therapy -- Cell Genesys Factor VII -- Novo Nordisk, Bayer, Baxter Intl. Factor VIIa -- PPL Therapeutics, ZymoGenetics Factor VIII - Bayer Genentech, Beaufour-Ipsen, CLB, Inex, Octagen, Pharmacia, **Pharming** Factor VIII -- PEGylated -- Bayer Factor VIII fragments -- Pharmacia Factor VIII gene therapy -- Targeted Genetics Factor VIII sucrose formulation – Bayer, Genentech Factor VIII-2 -- Bayer Factor VIII-3 -- Bayer Factor Xa inhibitors - Merck, Novo Nordisk, Mochida Factor XIII -- ZymoGenetics Factors VIII and IX gene therapy -- Genetics Institute/Targeted Genetics Famoxin -- Genset Fas TR -- Human Genome Sciences Felvizumab -- Scotgen FFR-VIIa -- Novo Nordisk FG-001 - F-Gene FG-002 - F-Gene FG-004 – F-Gene FG-005 - F-Gene FGF + fibrin -- Repair Fibrimage -- Bio-Tech. General fibrin-binding peptides - ISIS Innovation fibrinogen -- PPL Therapeutics, Pharming fibroblast growth factor - Chiron, NYU, Ramot, ZymoGenetics fibrolase conjugate -- Schering AG Filgrastim -- Amgen filgrastim -- PDA modified -- Xencor FLT-3 ligand -- Immunex FN18 CRM9 -

FIG. 28K

Glucocerebrosidase -- Genzyme follistatin -- Biotech Australia, Human glutamate decarboxylase -- Genzyme **Therapeutics** Transgenics follitropin alfa – Alkermes, ProLease, Glycoprotein S3 -- Kureha PowderJect, Serono, Akzo Nobel GM-CSF -- Immunex Follitropin Beta – Bayer, Organon GM-CSF tumour vaccine -- PowderJect FP 59 **GnRH** immunotherapeutic -- Protherics FSH -- Ferring Goserelin (LhRH antagonist) -- AstraZeneca FSH + LH -- Ferring gp75 antigen -- ImClone F-spondin -- CeNeS gp96 -- Antigenics fusion protein delivery system -- UAB GPI 0100 -- Galenica Research Foundation GR 4991W93 -- GlaxoSmithKline fusion toxins -- Boston Life Sciences Granulocyte colony-stimulating factor --G 5598 -- Genentech Dong-A GA-II -- Transkaryotic Therapies Gamma-interferon analogues -- SRC VB Granulocyte colony-stimulating factor conjugate VECTOR grass allergy therapy -- Dynavax Ganirelix -- Roche **GRF1-44 -- ICN** gastric lipase -- Meristem Growth Factor – Chiron, Atrigel, Atrix, Gavilimomab -Innogenetics, ZymoGenetics, Novo G-CSF - Amgen, SRC VB VECTOR growth factor peptides -- Biotherapeutics GDF-1 -- CeNeS growth hormone -- LG Chem GDF-5 -- Biopharm GDNF (glial derived neurotrophic factor) -growth hormone, Recombinant human --Serono Amgen GT 4086 -- Gliatech gelsolin -- Biogen GW 353430 -- GlaxoSmithKline Gemtuzumab ozogamicin -- Celltech GW-278884 -- GlaxoSmithKline Gene-activated epoetin-alfa -- Aventis H 11 -- Viventia Biotech Pharma -- Transkaryotic Therapies Glanzmann thrombasthenia gene therapy - H5N1 influenza A virus vaccine -- Protein Sciences Glatiramer acetate -- Yeda haemoglobin -- Biopure glial growth factor 2 -- CeNeS haemoglobin 3011, Recombinant -- Baxter GLP-1 – Amylin, Suntory, TheraTech, Healthcare Watson haemoglobin crosfumaril – Baxter Intl. GLP-1 peptide analogues – Zealand haemoglobin stabilized -- Ajinomoto **Pharaceuticals** haemoglobin, recombinant -- Apex GLP-2 - Novo Nordisk, Ontario, Inc., HAF -- Immune Response **Suntory Limited** Hantavirus vaccine glucagon -- Eli Lilly, ZymoGenetics Glucagon-like peptide-1 7-36 amide --**HB** 19 HBNF -- Regeneron Suntory HCC-1 -- Pharis Glucogen-like peptide -- Amylin

FIG. 28L

hCG -- Milkhaus hCG vaccine -- Zonagen HE-317 -- Hollis-Eden Pharmaceuticals Heat shock protein cancer and influenza vaccines -- StressGen Helicobacter pylori vaccine -- Acambis, AstraZeneca/CSL, Chiron, Provalis Helistat-G -- GalaGen Hemolink -- Hemosol hepapoietin -- Snow Brand heparanase -- InSight heparinase I -- Ibex heparinase III -- Ibex Hepatitis A vaccine -- American Biogenetic HIP-- Altachem Sciences Hepatitis A vaccine inactivated Hepatitis A vaccine Nothav -- Chiron Hepatitis A-hepatitis B vaccine --GlaxoSmithKline hepatitis B therapy -- Tripep Hepatitis B vaccine - Amgen, Chiron SpA, Meiji Milk, NIS, Prodeva, PowderJect, Rhein Biotech Hepatitis B vaccine recombinant -- Evans Vaccines, Epitec Combiotech, Genentech, Aventis Pasteur, Oncogen, Hyland MedImmune, Merck Sharp & Dohme, Rhein Biotech, Shantha Biotechnics, Vector, Yeda Hepatitis B vaccine recombinant TGP 943 -- HIV immune globulin - Abbott, Chiron Takeda Hepatitis C vaccine -- Bavarian Nordic, Chiron, Innogenetics Acambis, Hepatitis D vaccine -- Chiron Vaccines Hepatitis E vaccine recombinant --Genelabs/GlaxoSmithKline, Novavax hepatocyte growth factor - Panorama, Sosei hepatocyte growth factor kringle fragments -- EntreMed

Her-2/Neu peptides -- Corixa

Herpes simplex glycoprotein DNA vaccine – Merck, Wyeth-Lederle Vaccines-Malvern, Genentech, GlaxoSmithKline, Chiron, Takeda Herpes simplex vaccine -- Cantab Pharmaceuticals, CEL-SCI, Henderson Morley Herpes simplex vaccine live -- ImClone Systems/Wyeth-Lederle, Aventis Pasteur HGF derivatives -- Dompe hIAPP vaccine -- Crucell Hib-hepatitis B vaccine -- Aventis Pasteur HIC 1 Hirudins - Biopharma, Cangene, Dongkook, Japan Energy Corporation, Pharmacia Corporation, SIR International, Sanofi-Synthelabo, Sotragene, Rhein Biotech HIV edible vaccine -- ProdiGene HIV gp120 vaccine - Chiron, Ajinomoto, GlaxoSmithKline, ID Vaccine, Progenics, VaxGen HIV gp120 vaccine gene therapy -HIV gp160 DNA vaccine - PowderJect, Immuno, Protein Sciences HIV gp41 vaccine -- Panacos HIV HGP-30W vaccine -- CEL-SCI HIV peptides -- American Home Products HIV vaccine -- Applied bioTech., Axis Genetics, Biogen, Bristol-Myers Squibb, Genentech, Korea Green Cross, NIS, Oncogen, Protein Sciences Corporation, Terumo, Tonen Corporation, Wyeth-Ayerst, Wyeth-Lederle Vaccines-Malvern, Advanced BioScience Laboratories, Bavarian Nordic, Bavarian Nordic/Statens Serum Institute, GeneCure, Immune Response, Progenics, Therion Biologics,

United Biomedical, Chiron

Human monoclonal antibodies --HIV vaccine vCP1433 -- Aventis Pasteur HIV vaccine vCP1452 -- Aventis Pasteur Medarex/Northwest Biotherapeutics, Medarex/Seattle Genetics HIV vaccine vCP205 -- Aventis Pasteur human netrin-1 -- Exelixis HL-9 -- American BioScience human papillomavirus antibodies -- Epicyte HM-9239 -- Cytran Human papillomavirus vaccine -- Biotech HML-103 -- Hemosol Australia, IDEC, StressGen HML-104 -- Hemosol Human papillomavirus vaccine MEDI 501 --HML-105 -- Hemosol MedImmune/GlaxoSmithKline HML-109 -- Hemosol Human papillomavirus vaccine MEDI HML-110 - Hemosol 503/MEDI 504 --HML-121 -- Hemosol MedImmune/GlaxoSmithKline hNLP -- Pharis Human papillomavirus vaccine TA-CIN -Hookworm vaccine Cantab Pharmaceuticals host-vector vaccines -- Henogen Human papillomavirus vaccine TA-HPV --HPM 1 -- Chugai Cantab Pharmaceuticals HPV vaccine -- MediGene Human papillomavirus vaccine TH-GW --HSA -- Meristem Cantab/GlaxoSmithKline HSF -- StressGen human polyclonal antibodies -- Biosite/Eos HSP carriers -Weizmann, Yeda, Peptor BioTech./ Medarex HSPPC-70 -- Antigenics HSPPC-96, pathogen-derived -- Antigenics human type II anti factor VIII monoclonal antibodies -- ThromboGenics HSV 863 -- Novartis humanised anti glycoprotein lb murine HTLV-I DNA vaccine monoclonal antibodies -- ThromboGenics HTLV-I vaccine HumaRAD -- Intracell HTLV-II vaccine -- Access HuMax EGFR -- Genmab HU 901 -- Tanox HuMax-CD4 -- Medarex Hu23F2G -- ICOS HuMax-IL15 -- Genmab HuHMFG1 HYB 190 -- Hybridon HumaLYM -- Intracell Human krebs statika -- Yamanouchi HYB 676 -- Hybridon human monoclonal antibodies --I-125 MAb A33 -- Celltech Ibritumomab tiuxetan -- IDEC Abgenix/Biogen, Abgenix/ Corixa, IBT-9401 -- Ibex Abgenix/Immunex, Abgenix/Lexicon, IBT-9402 -- lbex Abgenix/ Pfizer, Athersys/Medarex. IC 14 -- ICOS Biogen/MorphoSys, CAT/Searle, Centocor/Medarex, Corixa/Kirin Brewery. Idarubicin anti-Ly-2.1 – **IDEC 114 -- IDEC** Corixa/Medarex, Eos BioTech./Medarex, Eos/Xenerex, Exelixis/Protein Design IDEC 131 -- IDEC **IDEC 152 -- IDEC** Labs, ImmunoGen/ Raven, Medarex/ **IDM 1 -- IDM** B.Twelve, MorphoSys/ImmunoGen, XTL

FIG. 28N

Biopharmaceuticals/Dyax,

IDPS -- Hollis-Eden Pharmaceuticals

iduronate-2-sulfatase -- Transkaryotic **Therapies** IGF/IBP-2-13 -- Pharis IGN-101 -- Igeneon IK HIR02 -- Iketon IL-11 -- Genetics Institute/AHP IL-13-PE38 -- NeoPharm IL-17 receptor -- Immunex IL-18BP -- Yeda IL-1Hy1 -- Hyseq IL-1ß -- Celltech IL-1ß adjuvant -- Celltech IL-2 -- Chiron IL-2 + IL-12 -- Hoffman La-Roche IL-6/sIL-6R fusion -- Hadasit IL-6R derivative -- Tosoh IL-7-Dap 389 fusion toxin - Ligand IL-21 - Novo Nordisk, ZymoGenetics IM-862 -- Cytran IMC-1C11 -- ImClone imiglucerase -- Genzyme Immune globulin intravenous (human) --Hoffman La Roche immune privilege factor -- Proneuron Immunocal -- Immunotec Immunogene therapy -- Briana Bio-Tech Immunoliposomal 5-fluorodeoxyuridinedipalmitate immunosuppressant vaccine -- Aixlie immunotoxin - Antisoma, NIH ImmuRAIT-Re-188 - Immunomedics imreg-1 -- Imreg infertility -- Johnson & Johnson, E-TRANS Infliximab -- Centocor Influenza virus vaccine -- Aventis Pasteur, **Protein Sciences** inhibin -- Biotech Australia, Human **Therapeutics** Inhibitory G protein gene therapy INKP-2001 -- InKine Inolimomab -- Diaclone

insulin -- AutoImmune, Altea, Biobras, BioSante, Bio-Tech, General, Chong Kun Dang, Emisphere, Flamel, Provalis, Rhein Biotech, TranXenoGen insulin (bovine) -- Novartis insulin analogue -- Eli Lilly Insulin Aspart -- Novo Nordisk insulin detemir -- Novo Nordisk insulin glargine -- Aventis insulin inhaled - Inhale Therapeutics Systems, Alkermes insulin oral -- Inovax insulin, AeroDose -- AeroGen insulin, AERx -- Aradigm insulin, BEODAS -- Elan insulin, Biphasix -- Helix insulin, buccal -- Generex insulin, I2R -- Flemington insulin, intranasal -- Bentley insulin, oral - Nobex, Unigene insulin, Orasome -- Endorex insulin, ProMaxx -- Epic insulin, Quadrant -- Elan insulin, recombinant -- Aventis insulin, Spiros -- Elan insulin, Transfersome -- IDEA insulin, Zymo, recombinant -- Novo Nordisk insulinotropin -- Scios Insulysin gene therapy integrin antagonists -- Merck interferon (Alpha2) -- SRC VB VECTOR, Viragen, Dong-A, Hoffman La-Roche, Genentech interferon - BioMedicines, Human Genome Sciences interferon (Alfa-n3)—Interferon Sciences intl. interferon (Alpha), Biphasix -- Helix

FIG. 280

interferon (Alpha)—Amgen, BioNative, Novartis, Genzyme Transgenics, Hayashibara, Inhale Therapeutics Systems, Medusa, Flamel, Dong-A, GeneTrol, Nastech, Shantha, Wassermann, LG Chem, Sumitomo, Aventis, Behring EGIS, Pepgen, Servier, Rhein Biotech, interferon (Alpha2A) interferon (Alpha2B) - Enzon, Schering-Plough, Biogen, IDEA interferon (Alpha-N1) -- GlaxoSmithKline interferon (beta) - Rentschler, GeneTrol, Meristem, Rhein Biotech, Toray, Yeda, Daiichi, Mochida interferon (Beta1A) - Serono, Biogen interferon (beta1A), inhale -- Biogen interferon (ß1b)-- Chiron interferon (tau) -- Pepgen Interferon alfacon-1 -- Amgen Interferon alpha-2a vaccine Interferon Beta 1b -- Schering/Chiron, InterMune Interferon Gamma -- Boehringer Ingelheim, interleukin-13 antagonists -- AMRAD Sheffield, Rentschler, Hayashibara interferon receptor, Type I -- Serono interferon(Gamma1B) -- Genentech Interferon-alpha-2b + ribavirin - Biogen, **ICN** Interferon-alpha-2b gene therapy --Schering-Plough Interferon-con1 gene therapy interleukin-1 antagonists -- Dompe Interleukin-1 receptor antagonist -- Abbott Bioresearch, Pharmacia Interleukin-1 receptor type I -- Immunex interleukin-1 receptor Type II -- Immunex Interleukin-1 trap -- Regeneron Interleukin-1-alpha -- Immunex/Roche interleukin-2 -- SRC VB VECTOR, Aiinomoto, Biomira, Chiron

IL-2/ diphtheria toxin -- Ligand Interleukin-3 -- Cangene Interleukin-4 -- Immunology Ventures, Sanofi Winthrop, Schering-Plough, Immunex/ Sanofi Winthrop, Bayer, Ono interleukin-4 + TNF-Alpha -- NIH interleukin-4 agonist -- Bayer interleukin-4 fusion toxin -- Ligand Interleukin-4 receptor - Immunex, Immun Interleukin-6 - Ajinomoto, Cangene, Yeda, Genetics Institute, Novartis interleukin-6 fusion protein interleukin-6 fusion toxin - Ligand, Serono interleukin-7 -- IC Innovations interleukin-7 receptor -- Immunex interleukin-8 antagonists -- Kyowa Hakko/Millennium/Pfizer interleukin-9 antagonists -- Genaera Interleukin-10 - DNAX, Schering-Plough Interleukin-10 gene therapy interleukin-12 -- Genetics Institute, Hoffman La-Roche interleukin-13 -- Sanofi Interleukin-13-PE38QQR interleukin-15 -- Immunex interleukin-16 -- Research Corp interleukin-18 -- GlaxoSmithKline Interleukin-18 binding protein -- Serono lor-P3 -- Center of Molecular Immunology IP-10 -- NIH IPF -- Metabolex IR-501 -- Immune Response ISIS 9125 - Isis Pharmaceuticals ISURF No. 1554 -- Millennium ISURF No. 1866 – Iowa State Univer. ITF-1697 -- Italfarmaco IxC 162 -- Ixion J 695 -- Cambridge Antibody Tech., Genetics Inst., Knoll

FIG. 28P

Jagged + FGF -- Repair

JKC-362 -- Phoenix Pharmaceuticals leptin, 2nd-generation -- Amgen leridistim -- Pharmacia JTP-2942 – Japan Tobacce leuprolide, ProMaxx -- Epic Juman monoclonal antibodies -leuprorelin, oral -- Unigene Medarex/Raven K02 -- Axys Pharmaceuticals LeuTech -- Papatin LEX 032 -- SuperGen Keliximab -- IDEC LiDEPT -- Novartis Keyhole limpet haemocyanin Lintuzumab (anti-CD33 MAb) -- Protein KGF -- Amgen Design Labs KM 871 -- Kyowa lipase -- Altus Biologics **KPI 135 -- Scios** lipid A vaccine -- EntreMed **KPI-022** -- Scios lipid-linked anchor Tech. - ICRT, ID Kringle 5 Biomedical KSB 304 liposome-CD4 Tech. -- Sheffield KSB-201 -- KS Biomedix Listeria monocytogenes vaccine L 696418 -- Merck LMB 1 L 703801 -- Merck LMB 7 L1 -- Acorda LMB 9 -- Battelle Memorial Institute, NIH L-761191 -- Merck LM-CD45 -- Cantab Pharmaceuticals lactoferrin – Meristem, Pharming, Agennix Iovastatin -- Merck lactoferrin cardio -- Pharming LSA-3 LAG-3 -- Serono LT-ß receptor -- Biogen LAIT -- GEMMA lung cancer vaccine -- Corixa LAK cell cytotoxin -- Arizona lamellarins -- PharmaMar/University of lusupultide -- Scios L-Vax -- AVAX Malaga LY 355455 -- Eli Lilly laminin A peptides -- NIH LY 366405 -- Eli Lilly lanoteplase -- Genetics Institute LY-355101 -- Eli Lilly laronidase -- BioMarin Lyme disease DNA vaccine -- Vical/Aventis Lassa fever vaccine Pasteur LCAT -- NIH Lyme disease vaccine -- Aquila LDP 01 -- Millennium Biopharmaceuticals, Aventis, Pasteur, LDP 02 -- Millennium Symbicom, GlaxoSmithKline, Hyland Lecithinized superoxide dismutase --Immuno, MedImmune Seikagaku Lymphocytic choriomeningitis virus vaccine LeIF adjuvant -- Corixa lymphoma vaccine - Biomira, Genitope leishmaniasis vaccine -- Corixa LYP18 lenercept -- Hoffman La-Roche lys plasminogen, recombinant Lenograstim – Aventis, Chugai Lysosomal storage disease gene therapy -lepirudin -- Aventis Avigen leptin - Amgen, IC Innovations lysostaphin -- Nutrition 21 Leptin gene therapy -- Chiron Corporation

FIG. 28Q

M 23 -- Gruenenthal M1 monoclonal antibodies -- Acorda Therapeutics MA 16N7C2 - Corvas Intl. malaria vaccine -- GlaxoSmithKline, AdProTech, Antigenics, Apovia, Aventis Pasteur, Axis Genetics, Behringwerke, CDCP, Chiron Vaccines, Genzyme Transgenics, Hawaii, MedImmune, NIH, NYU, Oxxon, Roche/Saramane, Biotech Australia, Rx Tech Malaria vaccine CDC/NIIMALVAC-1 malaria vaccine, multicomponent mammaglobin -- Corixa mammastatin -- Biotherapeutics mannan-binding lectin -- Natlmmu mannan-MUC1 -- Psiron **MAP 30** Marinovir -- Phytera MARstem -- Maret MB-015 -- Mochida MBP -- ImmuLogic MCI-028 -- Mitsubishi-Tokyo MCIF -- Human Genome Sciences MDC -- Advanced BioScience -- Akzo Nobel, ICOS MDX 11 -- Medarex MDX 210 -- Medarex MDX 22 -- Medarex MDX 22 MDX 240 -- Medarex **MDX 33** MDX 44 -- Medarex MDX 447 -- Medarex MDX H210 -- Medarex MDX RA -- Houston BioTech., Medarex ME-104 -- Pharmexa Measles vaccine Mecasermin -- Cephalon/Chiron, Chiron MEDI 488 -- MedImmune **MEDI 500**

MEDI 507 -- BioTransplant melanin concentrating hormone --**Neurocrine Biosciences** melanocortins -- OMRF Melanoma monoclonal antibodies -- Viragen melanoma vaccine -- GlaxoSmithKline, Akzo Nobel, Avant, Aventis Pasteur, Bavarian Nordic, Biovector, CancerVax, Genzyme Molecular Oncology, Humbolt, ImClone Systems, Memorial, NYU, Oxxon Melanoma vaccine Magevac -- Therion memory enhancers -- Scios meningococcal B vaccine -- Chiron meningococcal vaccine -- CAMR Meningococcal vaccine group B conjugate -- North American Vaccine Meningococcal vaccine group B recombinant -- BioChem Vaccines, Microscience Meningococcal vaccine group Y conjugate -- North American Vaccine Meningococcal vaccine groups A B and C conjugate -- North American Vaccine Mepolizumab -- GlaxoSmithKline Metastatin – EntreMed, Takeda Met-CkB7 -- Human Genome Sciences met-enkephalin -- TNI METH-1 -- Human Genome Sciences methioninase -- AntiCancer Methionine lyase gene therapy --AntiCancer Met-RANTES - Genexa Biomedical, Serono Metreleptin Microtubule inhibitor MAb Immunogen/Abgenix MGDF -- Kirin MGV -- Progenics micrin -- Endocrine microplasmin -- ThromboGenics MIF -- Genetics Institute

FIG. 28R

| migration inhibitory factor NIH | MAb 45-2D9- – haematoporphyrin |
|---|---------------------------------------|
| Mim CD4.1 – Xycte Therapies | conjugate |
| mirostipen Human Genome Sciences | MAb 4B4 |
| Mitumomab (BEC-2) – ImClone Systems, | MAb 4E3-CPA conjugate BCM Oncologia |
| Merck KGaA | MAb 4E3-daunorubicin conjugate |
| MK 852 Merck | MAb 50-6 |
| MLN 1202 (Anti-CCR2 monoclonal | MAb 50-61A – Institut Pasteur |
| antibody) – Millenium Pharmaceuticals | MAb 5A8 Biogen |
| Mobenakin NIS | MAb 791T/36-methotrexate conjugate |
| molgramostim Genetics Institute, Novartis | s MAb 7c11.e8 |
| monoclonal antibodies Abgenix/Celltech, | MAb 7E11 C5-selenocystamine conjugate |
| Immusol/ Medarex, Viragen/ Roslin | MAb 93KA9 Novartis |
| Institute, Cambridge Antibody Tech./Elan | MAb A5B7-cisplatin conjugate |
| MAb 108 – | Biodynamics Research, Pharmacia |
| MAb 10D5 | MAb A5B7-I-131 |
| MAb 14.18-interleukin-2 immunocytokine | MAb A7 |
| Lexigen | MAb A717 Exocell |
| MAb 14G2a – | MAb A7-zinostatin conjugate |
| MAb 15A10 – | MAb ABX-RB2 Abgenix |
| MAb 170 Biomira | MAb ACA 11 |
| MAb 177Lu CC49 | MAb AFP-I-131 – Immunomedics |
| MAb 17F9 | MAb AP1 |
| MAb 1D7 | MAb AZ1 |
| MAb 1F7 – Immune Network | MAb B3-LysPE40 conjugate |
| MAb 1H10-doxorubicin conjugate | MAb B4 – United Biomedical |
| MAb 26-2F | MAb B43 Genistein-conjugate |
| MAb 2A11 | MAb B43.13-Tc-99m Biomira |
| MAb 2E1 RW Johnson | MAb B43-PAP conjugate |
| MAb 2F5 | MAb B4G7-gelonin conjugate |
| MAb 31.1 International Biolmmune | MAb BCM 43-daunorubicin conjugate |
| Systems | BCM Oncologia |
| MAb 32 Cambridge Antibody Tech., | MAb BIS-1 |
| Peptech | MAb BMS 181170 Bristol-Myers Squibb |
| MAb 323A3 Centocor | MAb BR55-2 |
| MAb 3C5 | MAb BW494 |
| MAb 3F12 | MAb C 242-DM1 conjugate ImmunoGen |
| MAb 3F8 | MAb C242-PE conjugate |
| MAb 42/6 | MAb c30-6 |
| MAb 425 Merck KGaA | MAb CA208-cytorhodin-S conjugate |
| MAb 447-52D Merck Sharp & Dohme | Hoechst Japan |
| | MAb CC49 Enzon |
| | |

MAb LL2-I-131 – Immunomedics MAb ch14.18 -MAb CH14.18-GM-CSF fusion protein --MAb LL2-Y-90 MAb LS2D617 -- Hybritech Lexiden MAb LYM-1-gelonin conjugate MAb chCE7 MAb LYM-1-I-131 MAb CI-137 -- AMRAD MAb LYM-1-Y-90 MAb cisplatin conjugate MAb LYM-2 -- Peregrine MAb CLB-CD19 MAb M195 MAb CLB-CD19v MAb M195-bismuth 213 conjugate --MAb CLL-1 -- Peregrine Protein Design Labs MAb CLL-1-GM-CSF conjugate MAb CLL-1-IL-2 conjugate -- Peregrine MAb M195-gelonin conjugate MAb CLN IgG -- doxorubicin conjugates MAb M195-I-131 MAb M195-Y-90 MAb conjugates – Tanox MAb MA 33H1 -- Sanofi MAb D612 MAb MAD11 MAb Dal B02 MAb MGb2 MAb DC101 -- ImClone MAb MINT5 MAb EA 1 – MAb MK2-23 MAb EC708 -- Biovation MAb MOC31 ETA(252-613) conjugate MAb EP-5C7 -- Protein Design Labs MAb MOC-31-In-111 MAb ERIC-1 -- ICRT MAb MOC-31-PE conjugate MAb F105 gene therapy MAb MR6 -MAb FC 2.15 MAb MRK-16 -- Aventis Pasteur MAb G250 -- Centocor MAb MS11G6 MAb GA6 MAb MX-DTPA BrE-3 MAb GA733 MAb MY9 MAb Gliomab-H -- Viventia Biotech MAb Nd2 -- Tosoh MAb HB2-saporin conjugate MAb NG-1 -- Hygeia MAb HD 37 – MAb NM01 - Nissin Food MAb HD37-ricin chain-A conjugate MAb OC 125 MAb HNK20 -- Acambis MAb OC 125-CMA conjugate MAb huN901-DM1 conjugate --MAb OKI-1 -- Ortho-McNeil **ImmunoGen** MAb OX52 -- Bioproducts for Science MAb I-131 CC49 -- Corixa MAb PMA5 MAb ICO25 MAb PR1 MAb ICR12-CPG2 conjugate MAb prost 30 MAb ICR-62 MAb R-24 MAb IRac-ricin A conjugate MAb R-24 α Human GD3 -- Celltech MAb K1 MAb RFB4-ricin chain A conjugate MAb KS1-4-methotrexate conjugate MAb RFT5-ricin chain A conjugate MAb L6 -- Bristol-Myers Squibb, Oncogen MAb SC 1 MAb LiCO 16-88

Muc-1 vaccine -- Corixa MAb SM-3 -- ICRT mucosal tolerance -- Aberdeen MAb SMART 1D10 -- Protein Design Labs mullerian inhibiting subst MAb SMART ABL 364 -- Novartis muplestim - Genetics Institute, Novartis, MAb SN6f DSM Anti-Infectives MAb SN6f-deglycosylated ricin A chain murine MAb -- KS Biomedix conjugate -Mutant somatropin -- JCR Pharmaceutical MAb SN6i MV 833 -- Toagosei MAb SN7-ricin chain A conjugate Mycoplasma pulmonis vaccine MAb T101-Y-90 conjugate -- Hybritech Mycoprex -- XOMA MAb T-88 -- Chiron myeloperoxidase -- Henogen MAb TB94 -- Cancer ImmunoBiology myostatin -- Genetics Institute MAb TEC 11 Nacolomab tafenatox -- Pharmacia MAb TES-23 -- Chugai Nagrecor -- Scios MAb TM31 -- Avant MAb TNT-1 -- Cambridge Antibody Tech., nagrestipen -- British Biotech NAP-5 - Corvas Intl. Peregrine NAPc2 - Corvas Intl. MAb TNT-3 nartograstim -- Kyowa MAb TNT-3 -- IL2 fusion protein -Natalizumab -- Protein Design Labs MAb TP3-At-211 Nateplase – NIH, Nihon Schering MAb TP3-PAP conjugate – nateplase -- Schering AG MAb UJ13A -- ICRT NBI-3001 -- Neurocrine Biosci. MAb UN3 NBI-5788 -- Neurocrine Biosci. MAb ZME-018-gelonin conjugate NBI-6024 -- Neurocrine Biosci. MAb-BC2 -- GlaxoSmithKline Nef inhibitors -- BRI MAb-DM1 conjugate -- ImmunoGen Neisseria gonorrhoea vaccine -- Antex MAb-ricin-chain-A conjugate -- XOMA Biologics MAb-temoporfin conjugates Neomycin B-arginine conjugate Monopharm C -- Viventia Biotech Nerelimomab -- Chiron monteplase -- Eisai Nerve growth factor - Amgen - Chiron, montirelin hydrate -- Gruenenthal Genentech moroctocog alfa - Genetics Institute Nerve growth factor gene therapy Moroctocog-alfa -- Pharmacia nesiritide citrate -- Scios MP 4 neuregulin-2 -- CeNeS MP-121 -- Biopharm neurocan -- NYU MP-52 -- Biopharm neuronal delivery system -- CAMR MRA -- Chugai Neurophil inhibitory Factor -- Corvas MS 28168 -- Mitsui Chemicals, Nihon Neuroprotective vaccine -- University of Schering Auckland MSH fusion toxin -- Ligand neurotrophic chimaeras -- Regeneron MSI-99 -- Genaera neurotrophic factor - NsGene, CereMedix MT 201 -- Micromet

Oncophage -- Antigenics

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NeuroVax -- Immune Response neurturin -- Genentech neutral endopeptidase -- Genentech NGF enhancers -- NeuroSearch NHL vaccine -- Large Scale Biology NIP45 -- Boston Life Sciences NKI-B20 NM 01 – Nissin Food NMI-139 -- NitroMed NMMP -- Genetics Institute NN-2211 -- Novo Nordisk Noggin -- Regeneron Nonacog alfa Norelin -- Biostar Norwalk virus vaccine NRLU 10 -- NeoRx NRLU 10 PE -- NeoRx NT-3 -- Regeneron NT-4/5 -- Genentech NU 3056 NU 3076 NX 1838 -- Gilead Sciences NY ESO-1/CAG-3 antigen -- NIH NYVAC-7 -- Aventis Pasteur NZ-1002 -- Novazyme obesity therapy -- Nobex OC 10426 -- Ontogen OC 144093 -- Ontogen OCIF -- Sankyo Oct-43 -- Otsuka Odulimomab -- Immunotech OK PSA - liposomal OKT3-gamma-1-ala-ala OM 991 OM 992 Omalizumab -- Genentech oncoimmunin-L -- NIH Oncolysin B -- ImmunoGen Oncolysin CD6 -- ImmunoGen Oncolysin M -- ImmunoGen Oncolysin S -- ImmunoGen

Oncostatin M -- Bristol-Myers Squibb OncoVax-CL -- Jenner Biotherapies OncoVax-P -- Jenner Biotherapies onercept -- Yeda onychomycosis vaccine -- Boehringer Ingelheim opebecan -- XOMA opioids -- Arizona Oprelvekin -- Genetics Institute Oregovomab -- AltaRex Org-33408 b-- Akzo Nobel Orolip DP -- EpiCept oryzacystatin OSA peptides - GenSci Regeneration osteoblast-cadherin GF -- Pharis Osteocalcin-thymidine kinase gene therapy osteogenic protein -- Curis osteopontin -- OraPharma osteoporosis peptides - Integra, Telios osteoprotegerin - Amgen, SnowBrand otitis media vaccines -- Antex Biologics ovarian cancer -- University of Alabama OX40-IgG fusion protein -- Cantab, Xenova P 246 -- Diatide P 30 -- Alfacell p1025 -- Active Biotech P-113[^] -- Demegen P-16 peptide -- Transition Therapeutics p43 -- Ramot P-50 peptide -- Transition Therapeutics p53 + RAS vaccine -- NIH, NCI PACAP(1-27) analogue paediatric vaccines -- Chiron Pafase -- ICOS PAGE-4 plasmid DNA -- IDEC PAI-2 -- Biotech Australia, Human Therapeutics Palifermin (keratinocyte growth factor) --Amgen Palivizumab -- MedImmune

FIG. 28V

PAM 4 -- Merck pamiteplase -- Yamanouchi pancreatin, Minitabs -- Eurand Pangen -- Fournier Pantarin - Selective Genetics Parainfluenza virus vaccine - Pharmacia, Pierre Fabre paraoxanase -- Esperion parathyroid hormone - Abiogen, Korea **Green Cross** Parathyroid hormone (1-34) --Chugai/Suntory Parkinson's disease gene therapy -- Cell Genesys/ Ceregene Parvovirus vaccine -- MedImmune PCP-Scan - Immunomedics PDGF -- Chiron PDGF cocktail -- Theratechnologies peanut allergy therapy -- Dynavax PEG anti-ICAM MAb -- Boehringer Ingelheim PEG asparaginase -- Enzon PEG glucocerebrosidase PEG hirudin - Knoll PEG interferon-alpha-2a -- Roche PEG interferon-alpha-2b + ribavirin -Biogen, Enzon, ICN Pharmaceuticals, Schering-Plough PEG MAb A5B7 -Pegacaristim - Amgen -- Kirin Brewery --ZymoGenetics Pegaldesleukin -- Research Corp pegaspargase -- Enzon pegfilgrastim -- Amgen PEG-interferon Alpha -- Viragen PEG-interferon Alpha 2A -- Hoffman La-Roche PEG-interferon Alpha 2B -- Schering-Plough Tokyo PEG-r-hirudin -- Abbott PEG-rHuMGDF -- Amgen

PEG-uricase -- Mountain View Pegvisomant – Genentech PEGylated proteins, PolyMASC -- Valentis PEGylated recombinant native human leptin -- Roche Pemtumomab Penetratin -- Cyclacel Pepscan – Antisoma peptide G - Peptech, ICRT peptide vaccine -- NIH, NCI Pexelizumab pexiganan acetate -- Genaera Pharmaprojects No. 3179 -- NYU Pharmaprojects No. 3390 -- Ernest Orlando Pharmaprojects No. 3417 -- Sumitomo Pharmaprojects No. 3777 -- Acambis Pharmaprojects No. 4209 -- XOMA Pharmaprojects No. 4349 - Baxter Intl. Pharmaprojects No. 4651 Pharmaprojects No. 4915 -- Avanir Pharmaprojects No. 5156 -- Rhizogenics Pharmaprojects No. 5200 -- Pfizer Pharmaprojects No. 5215 -- Origene Pharmaprojects No. 5216 -- Origene Pharmaprojects No. 5218 -- Origene Pharmaprojects No. 5267 - ML Laboratories Pharmaprojects No. 5373 -- MorphoSys Pharmaprojects No. 5493 -- Metabolex Pharmaprojects No. 5707 -- Genentech Pharmaprojects No. 5728 -- Autogen Pharmaprojects No. 5733 -- BioMarin Pharmaprojects No. 5757 -- NIH Pharmaprojects No. 5765 -- Gryphon Pharmaprojects No. 5830 -- AntiCancer Pharmaprojects No. 5839 -- Dyax Pharmaprojects No. 5849 -- Johnson & Johnson Pharmaprojects No. 5860 -- Mitsubishi-

FIG. 28W

Plasminogen activators -- Abbott Pharmaprojects No. 5869 – Oxford Laboratories, American Home Products, **GlycoSciences** Boehringer Mannheim, Chiron Pharmaprojects No. 5883 -- Asahi Brewery Corporation, DuPont Pharmaceuticals, Eli Pharmaprojects No. 5947 -- StressGen Lilly, Shionogi, Genentech, Genetics Pharmaprojects No. 5961 --Institute, GlaxoSmithKline, Hemispherx Theratechnologies Biopharma, Merck & Co, Novartis, Pharmaprojects No. 5962 -- NIH Pharmacia Corporation, Wakamoto, Yeda Pharmaprojects No. 5966 -- NIH plasminogen-related peptides -- Bio-Tech. Pharmaprojects No. 5994 -- Pharming General/MGH Pharmaprojects No. 5995 -- Pharming platelet factor 4 -- RepliGen Pharmaprojects No. 6023 -- IMMUCON Platelet-derived growth factor - Amgen --Pharmaprojects No. 6063 -- Cytoclonal ZymoGenetics Pharmaprojects No. 6073 -- SIDDCO plusonermin-- Hayashibara Pharmaprojects No. 6115 -- Genzyme PMD-2850 -- Protherics Pharmaprojects No. 6227 -- NIH Pneumococcal vaccine -- Antex Biologics, Pharmaprojects No. 6230 -- NIH **Aventis Pasteur** Pharmaprojects No. 6236 -- NIH Pneumococcal vaccine intranasal --Pharmaprojects No. 6243 -- NIH BioChem Vaccines/Biovector Pharmaprojects No. 6244 -- NIH PR1A3 Pharmaprojects No. 6281 -- Senetek PR-39 Pharmaprojects No. 6365 -- NIH pralmorelin -- Kaken Pharmaprojects No. 6368 -- NIH Pretarget-Lymphoma -- NeoRx Pharmaprojects No. 6373 -- NIH Priliximab -- Centocor Pharmaprojects No. 6408 - Pan Pacific PRO 140 -- Progenics Pharmaprojects No. 6410 -- Athersys PRO 2000 -- Procept Pharmaprojects No. 6421 - Oxford PRO 367 -- Progenics **GlycoSciences** Pharmaprojects No. 6522 -- Maxygen PRO 542 -- Progenics pro-Apo A-I -- Esperion Pharmaprojects No. 6523 -- Pharis prolactin -- Genzyme Pharmaprojects No. 6538 -- Maxygen Prosaptide TX14(A) -- Bio-Tech. General Pharmaprojects No. 6554 -- APALEXO Pharmaprojects No. 6560 -- Ardana prostate cancer antbodies - Immunex, UroCor Pharmaprojects No. 6562 -- Bayer prostate cancer antibody therapy --Pharmaprojects No. 6569 -- Eos Genentech/UroGenesys, Phenoxazine Genotherapeutics Phenylase -- Ibex prostate cancer immunotherapeutics -- The Pigment epithelium derived factor plasminogen activator inhibitor-1, PSMA Development Company prostate cancer vaccine -- Aventis Pasteur, recombinant -- DuPont Pharmaceuticals Zonagen, Corixa, Dendreon, Jenner Biotherapies, Therion Biologics

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RD 62198 prostate-specific antigen -- EntreMed rDnase -- Genentech protein A -- RepliGen RDP-58 -- SangStat protein adhesives -- Enzon protein C - Baxter Intl., PPL Therapeutics, RecepTox-Fce -- Keryx RecepTox-GnRH - Keryx, MTR ZymoGenetics protein C activator - Gilead Sciences **Technologies** RecepTox-MBP - Keryx, MTR protein kinase R antags -- NIH **Technologies** protirelin -- Takeda recFSH -- Akzo Nobel, Organon protocadherin 2 -- Caprion Pro-urokinase - Abbott, Bristol-Myers REGA 3G12 Squibb, Dainippon, Tosoh -- Welfide Regavirumab -- Teijin P-selectin glycoprotein ligand-1 -- Genetics relaxin -- Connetics Corp Renal cancer vaccine -- Macropharm Institute repifermin -- Human Genome Sciences pseudomonal infections -- InterMune Respiratory syncytial virus PFP-2 vaccine --Pseudomonas vaccine -- Cytovax Wyeth-Lederle PSGL-Ig -- American Home Products Respiratory syncytial virus vaccine -PSP-94 -- Procyon GlaxoSmithKline, Pharmacia, Pierre Fabre PTH 1-34 -- Nobex Respiratory syncytial virus vaccine Quilimmune-M -- Antigenics inactivated R 744 -- Roche Respiratory syncytial virus-parainfluenza R 101933 virus vaccine -- Aventis Pasteur, R 125224 -- Sankyo Pharmacia RA therapy -- Cardion Reteplase -- Boehringer Mannheim, Rabies vaccine recombinant -- Aventis Hoffman La-Roche Pasteur, BioChem Vaccines, Kaketsuken Retropep -- Retroscreen **Pharmaceuticals** RFB4 (dsFv) PE38 RadioTheraClM -- YM BioSciences RFI 641 -- American Home Products Ramot project No. 1315 -- Ramot RFTS -- UAB Research Foundation Ramot project No. K-734A -- Ramot RG 12986 -- Aventis Pasteur Ramot project No. K-734B -- Ramot RG 83852 -- Aventis Pasteur Ranibizumab (Anti-VEGF fragment) --RG-1059 -- RepliGen Genentech rGCR -- NIH RANK -- Immunex rGLP-1 -- Restoragen ranpirnase -- Alfacell ranpirnase-anti-CD22 MAb -- Alfacell rGRF -- Restoragen rh Insulin – Eli Lilly RANTES inhibitor -- Milan RHAMM targeting peptides -- Cangene RAPID drug delivery systems -- ARIAD rHb1.1 - Baxter Intl. rasburicase -- Sanofi rhCC10 -- Claragen rBPI-21, topical -- XOMA rhCG -- Serono RC 529 -- Corixa Rheumatoid arthritis gene therapy rCFTR -- Genzyme Transgenics

Rheumatoid arthritis vaccine -- Veterans Affairs Medical Center rhLH -- Serono Ribozyme gene therapy -- Genset Rickettsial vaccine recombinant

RIP-3 -- Rigel

Rituximab -- Genentech RK-0202 -- RxKinetix RLT peptide -- Esperion

RIGScan CR -- Neoprobe

rM/NEI -- IVAX rmCRP -- Immtech RN-1001 -- Renovo RN-3 -- Renovo

RNAse conjugate -- Immunomedics

RO 631908 -- Roche

Rotavirus vaccine -- Merck
RP 431 -- DuPont Pharmaceuticals

RP-128 -- Resolution RPE65 gene therapy -

RPR 110173 -- Aventis Pasteur
RPR 115135 -- Aventis Pasteur
RPR 116258A -- Aventis Pasteur
rPSGL-Ig -- American Home Products
r-SPC surfactant -- Byk Gulden
RSV antibody -- Medimmune

Ruplizumab -- Biogen

rV-HER-2/neu -- Therion Biologics

SA 1042 -- Sankyo

sacrosidase - Orphan Medical

Sant 7

Sargramostim -- Immunex saruplase -- Gruenenthal Satumomab -- Cytogen SB 1 -- COR Therapeutics SB 207448 -- GlaxoSmithKline SB 208651 -- GlaxoSmithKline

SB 240683 -- GlaxoSmithKline SB 249415 -- GlaxoSmithKline

SB 249417 -- GlaxoSmithKline

SB 6 -- COR Therapeutics

SB RA 31012 -

SC 56929 -- Pharmacia

SCA binding proteins – Curis, Enzon scFv(14E1)-ETA Berlex Laboratories,

Schering AG ScFv(FRP5)-ETA – ScFv6C6-PE40 – SCH 55700 -- Celltech

Schistosomiasis vaccine -- Glaxo

Wellcome/Medeva, Brazil

SCPF -- Advanced Tissue Sciences scuPA-suPAR complex -- Hadasit

SD-9427 -- Pharmacia

SDF-1 -- Ono

SDZ 215918 -- Novartis SDZ 280125 -- Novartis SDZ 89104 -- Novartis SDZ ABL 364 -- Novartis SDZ MMA 383 -- Novartis Secretin -- Ferring, Repligen

serine protease inhibs -- Pharis sermorelin acetate -- Serono

SERP-1 -- Viron

sertenef -- Dainippon

serum albumin, Recombinant human --

Aventis Behring

serum-derived factor -- Hadasit

Sevirumab -- Novartis SGN 14 -- Seatle Genetics SGN 15 -- Seatle Genetics SGN 17/19 -- Seatle Genetics SGN 30 -- Seatle Genetics

SGN 30 -- Seatle Genetics
SGN-10 -- Seatle Genetics

SGN-11 -- Seatle Genetics

SH 306 -- DuPont Pharmaceuticals

Shanvac-B -- Shantha

Shigella flexneri vaccine - Avant, Acambis,

Novavax

Shigella sonnei vaccine -

sICAM-1 -- Boehringer Ingelheim

Silteplase -- Genzyme

FIG. 28Z

SIV vaccine - Endocon, Institut Pasteur SK 896 -- Sanwa Kagaku Kenkyusho SK-827 -- Sanwa Kagaku Kenkyusho Skeletex -- CellFactors SKF 106160 -- GlaxoSmithKline S-nitroso-AR545C -SNTP -- Active Biotech somatomedin-1 - GroPep, Mitsubishi-Tokyo, NIH somatomedin-1 carrier protein -- Insmed somatostatin -- Ferring Somatotropin/ Human Growth Hormone -- Bio-Tech. General, Eli Lilly somatropin -- Bio-Tech. General, Alkermes, SUIS-LHRH -- United Biomedical ProLease, Aventis Behring, Biovector, Cangene, Dong-A, Eli Lilly, Emisphere, Enact, Genentech, Genzyme Transgenics, YM BioSciences Novartis, Novo Nordisk, Pharmacia Serono, TranXenoGen somatropin derivative -- Schering AG somatropin, AIR -- Eli Lilly Somatropin, inhaled -- Eli Lilly/Alkermes somatropin, Kabi -- Pharmacia somatropin, Orasome -- Novo Nordisk Sonermin -- Dainippon Pharmaceutical SP(V5.2)C -- Supertek SPf66 sphingomyelinase -- Genzyme SR 29001 -- Sanofi SR 41476 -- Sanofi SR-29001 -- Sanofi SS1(dsFV)-PE38 -- NeoPharm ß2 microglobulin -- Avidex ß2-microglobulin fusion proteins -- NIH ß-amyloid peptides -- CeNeS ß-defensin -- Pharis Staphylococcus aureus infections --Inhibitex/ZLB

Staphylococcus aureus vaccine conjugate --Nabi Staphylococcus therapy -- Tripep Staphylokinase - Biovation, Prothera, Thrombogenetics Streptococcal A vaccine -- M6 Pharmaceuticals, North American Vaccine Streptococcal B vaccine -- Microscience Streptococcal B vaccine recombinant --Biochem Vaccines Streptococcus pyogenes vaccine STRL-33 -- NIH Subalin -- SRC VB VECTOR SUIS -- United Biomedical SUN-E3001 -- Suntory super high affinity monoclonal antibodies --Grandis/InfiMed, CSL, InfiMed, MacroMed, Superoxide dismutase - Chiron, Enzon, Ube Industries, Bio-Tech, Yeda superoxide dismutase-2 -- OXIS suppressin -- UAB Research Foundation SY-161-P5 -- ThromboGenics SY-162 -- ThromboGenics Systemic lupus erythematosus vaccine --MedClone/VivoRx T cell receptor peptides -- Xoma T cell receptor peptide vaccine T4N5 liposomes -- AGI Dermatics TACI, soluble -- ZymoGenetics targeted apoptosis -- Antisoma tasonermin -- Boehringer Ingelheim **TASP** TASP-V Tat peptide analogues -- NIH TBP I -- Yeda TBP II TBV25H -- NIH Tc 99m ior cea1 -- Center of Molecular **Immunology** Tc 99m P 748 -- Diatide

FIG. 28AA

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Tissue factor -- Genentech Tc 99m votumumab -- Intracell Tissue factor pathway inhibitor Tc-99m rh-Annexin V - Theseus Imaging TJN-135 -- Tsumura teceleukin -- Biogen TM 27 -- Avant tenecteplase -- Genentech TM 29 -- Avant Teriparatide -- Armour Pharmaceuticals, TMC-151 - Tanabe Seiyaku Asahi Kasei, Eli Lilly TNF tumour necrosis factor -- Asahi Kasei terlipressin -- Ferring TNF Alpha -- Cytimmune testisin -- AMRAD TNF antibody -- Johnson & Johnson Tetrafibricin -- Roche TNF binding protein -- Amgen TFPI -- EntreMed TNF degradation product -- Oncotech tgD-IL-2 -- Takeda TNF receptor -- Immunex TGF-Alpha -- ZymoGenetics TNF receptor 1, soluble -- Amgen TGF-ß -- Kolon TNF Tumour necrosis factor-alpha -- Asahi TGF-ß2 -- Insmed Kasei, Genetech, Mochida TGF-B3 -- OSI TNF-Alpha inhibitor -- Tripep Thalassaemia gene therapy -- Crucell TNFR:Fc gene therapy - Targeted Genetics TheraCIM-h-R3 -- Center of Molecular TNF-SAM2 Immunology, YM BioSciences ToleriMab -- Innogenetics Theradigm-HBV -- Epimmune Toxoplasma gondii vaccine --Theradigm-HPV -- Epimmune Theradigm-malaria -- Epimmune GlaxoSmithKline TP 9201 -- Telios Theradigm-melanoma -- Epimmune TP10 -- Avant TheraFab - Antisoma TP20 -- Avant ThGRF 1-29 -- Theratechnologies ThGRF 1-44 -- Theratechnologies tPA -- Centocor trafermin -- Scios Thrombin receptor activating peptide --TRAIL/Apo2L -- Immunex Abbott TRAIL-R1 MAb - Cambridge Antibody thrombomodulin - Iowa, Novocastra Thrombopoietin -- Dragon Pharmaceuticals, Technologies transferrin-binding proteins -- CAMR Genentech Transforming growth factor-beta-1 -thrombopoietin, Pliva -- Receptron Genentech Thrombospondin 2 transport protein -- Genesis thrombostatin -- Thromgen Trastuzumab -- Genetech thymalfasin -- SciClone TRH -- Ferring thymocartin - Gedeon Richter Triabin -- Schering AG thymosin Alpha1 -- NIH thyroid stimulating hormone -- Genzyme Triconal Triflavin tICAM-1 -- Bayer Tick anticoagulant peptide -- Merck troponin I -- Boston Life Sciences TRP-2[^] -- NIH

FIG. 28BB

trypsin inhibitor -- Mochida

TIF -- Xoma

Tifacogin - Chiron, NIS, Pharmacia

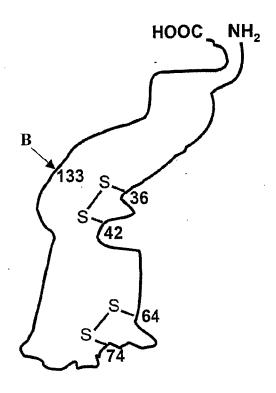
Vascular endothelial growth factors – R&D TSP-1 gene therapy -Systems TT-232 vascular targeting agents -- Peregrine TTS-CD2 -- Active Biotech vasopermeation enhancement agents --Tuberculosis vaccine -- Aventis Pasteur, Peregrine Genesis Tumor Targeted Superantigens -- Active vasostatin -- NIH VCL -- Bio-Tech. General Biotech -- Pharmacia VEGF - Genentech, Scios tumour vaccines -- PhotoCure tumour-activated prodrug antibody VEGF inhibitor -- Chugai VEGF-2 -- Human Genome Sciences conjugates -- Millennium/ImmunoGen VEGF-Trap -- Regeneron tumstatin -- ILEX viscumin, recombinant -- Madaus Tuvirumab -- Novartis Vitaxin TV-4710 – Teva Vitrase -- ISTA Pharmaceuticals TWEAK receptor -- Immunex West Nile virus vaccine -- Bavarian Nordic TXU-PAP WP 652 TY-10721 – TOA Eiyo WT1 vaccine -- Corixa Type I diabetes vaccine -- Research Corp WX-293 -- Wilex BioTech. Typhoid vaccine CVD 908 WX-360 -- Wilex BioTech. U 143677 -- Pharmacia WX-UK1 -- Wilex BioTech. U 81749 -- Pharmacia XMP-500 -- XOMA UA 1248 -- Arizona XomaZyme-791 -- XOMA UGIF -- Sheffield XTL 001 -- XTL Biopharmaceuticals UIC 2 XTL 002 -- XTL Biopharmaceuticals UK 101 veast delivery system -- Globelmmune UK-279276 - Corvas Intl. Yersinia pestis vaccine urodilatin -- Pharis YIGSR-Stealth -- Johnson & Johnson urofollitrophin -- Serono Yissum Project No. D-0460 -- Yissum Urokinase -- Abbott YM 207 -- Yamanouchi uteroferrin-- Pepgen YM 337 -- Protein Design Labs V 20 -- GLYCODesign Yttrium-90 labelled biotin V2 vasopressin receptor gene therapy Yttrium-90-labeled anti-CEA MAb T84.66 vaccines -- Active Biotech ZD 0490 – AstraZeneca Varicella zoster glycoprotein vaccine --Research Corporation Technologies ziconotide -- Elan Varicella zoster virus vaccine live -- Cantab ZK 157138 -- Berlex Laboratories Zolimomab aritox **Pharmaceuticals**

Vascular endothelial growth factor – Genentech, University of California

Zorcell -- Immune Response

ZRXL peptides -- Novartis

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{pmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, sialyl or oligosialyl

FIG. 29A

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CHO, BHK, 293 cells, Vero expressed G-CSF a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29B

Insect cell expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0.

- ↓ 1. Galactosyltransferase, UDP-Gal2. CMP-SA-PEG, ST3Gal1
- a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29C

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E. coli expressed G-CSF a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc▼ 2. CMP-SA-PEG, sialyltransferase
- c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 29D

NSO expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0

1. CMP-SA-levulinate, ST3Gal1
 2. H₄N₂-PEG

a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

FIG. 29E

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E. coli expressed G-CSF a-e = 0.

1. Endo-GalNAc-osaminidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c = 0; R = PEG.

FIG. 29F

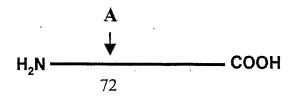
E. coli expressed G-CSF a-e = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e = 0 or 1; a,-c = 0; R = PEG.

FIG. 29G

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e} - \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f} - \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g} - \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h} - \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right]_{u} = aa} \end{bmatrix}_{bb}$$

a-d, i, n-u (independently selected) = 0 or 1.

aa, bb, cc, dd, ee (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

v-z = 0; R = modifying group, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 30A

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha 14C.

a-d, aa, bb = 1; e-h = 1 to 4; cc, j-m, i, r-u (independently selected) = 0 or 1; q, n-p, v-z, cc, dd, ee = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.
```

FIG. 30B

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0; e, g, i, r, t (independently selected) = 0 or 1; aa, bb = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.
```

FIG. 30C

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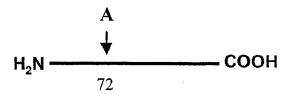
```
Yeast expressed interferon alpha-14C.
a-q, cc, dd, ee, v-z = 0;
r-y (independently selected) = 0 to 1;
aa, bb = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.
```

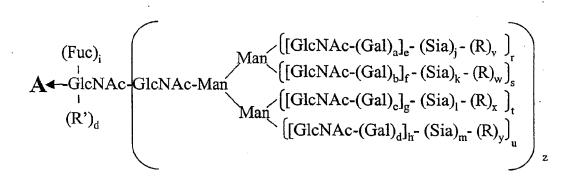
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

a-z, bb = 0; aa = 1; R' = -Gal-Sia-PEG.

FIG. 30D

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a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1. R = polymer; R' = sugar, glycoconjugate.

FIG. 30E

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;

a-g, j-m, i (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 30F

```
Insect cell or fungi expressed
interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 30G

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Yeast expressed interferon alpha-14C. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 30H

NSO expressed interferon alpha 14C. a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 301

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CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;

a-g, j-m, i (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1.

1. CMP-SA-PEG, α 2,8-ST

h = 1 to 3; a-g, i, r-u (independently selected) = 0 or 1; j-m (independently selected) = 0 to 2; v-y (independently selected) = 1, when j-m (independently selected) is 2; z = 1; n = 0; R = PEG.

FIG. 30J

CHO, BHK, 293 cells, Vero expressed Interferon alpha-14C.
a-g, j-m, r-u (independently selected) = 0 or 1; h = 1 to 3; n, v-y = 0; z = 1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 30K

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;

a-g, j-m, i (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1.
```

1. CMP-SA, α 2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 40;
z = 1; v-y, n = 0.
```

FIG. 30L

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. GNT's 1 & 2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1; z = 1; b, d, f, h, j-n, s, u, w, y = 0; R = transferrin.

FIG. 30M

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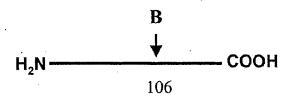
```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

```
i (independently selected) = 0 or 1;
a-h, j-m, r-z = 0;
n = 1; R' = -Gal-linker-transferrin.
```

FIG. 30N

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{GlcNAc-Gal})_{f_{\underline{-}}}(\operatorname{Sia})_{b} - (R)_{g} \\ -\operatorname{GalNAc-(Gal})_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{e}$$

a-c, e, f (independently selected) = 0 or 1; d, g = 0; R = polymer, glycoconjugate.

FIG. 300

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CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c (independently selected) = 0 or 1; e = 1; d, f, g = 0

1. Sia

1. Sialidase

2. CMP-SA-PEG, ST3Gal1

a-d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 30P

Insect cell expressed interferon alpha (2a or 2b). a, e (independently selected) = 0 or 1; b, c, d, f, g = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; b, f, g = 0; R = PEG.

FIG. 30Q

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E. coli expressed IF-alpha (2a or 2b). a-g=0.

 GalNAc Transferase, UDP-GalNAc-PEG

a-c, f, g = 0; d, e = 1; R = PEG.

FIG. 30R

NSO expressed IF-alpha (2a or 2b). a (independently selected) = 0 or 1; e = 1; b, c, d, f, g = 0

- 1. CMP-SA-levulinate, ST3Gal1
- $2. H_4N_2$ -PEG

a, c, d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 30S

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E. coli expressed IF-alpha (2a or 2b). a-g=0.

 Endo-N-acetylgalatosamidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c, f, g = 0; R = PEG.

FIG. 30T

E. coli expressed IF-alpha (2a or 2b). a-g=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. sialyltransferase, CMP-SA-PEG

b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 30U

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CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).

a-c, f (independently selected) = 0 or 1;

e = 1; d, g = 0

Sialidase

2. CMP-SA-PEG, ST3Gal1 and ST3Gal3

a-d, f, g (independently selected) = 0 or 1; e = 1; R = PEG.

FIG. 30V

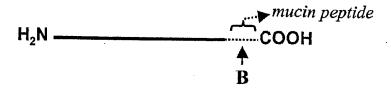
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e = 1; d, g = 0

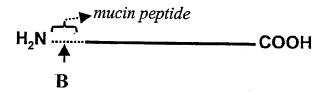
- 1. Sialidase
- 2. CMP-SA-linker-SA-CMP, ,ST3Gal1
- 3. ST3Gal3, transferrin

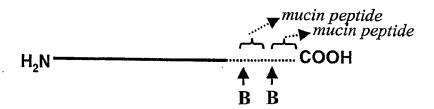
a-d, f (independently selected) = 0 or 1; e = 1; R = transferrin; g = 0.

FIG. 30W

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (\operatorname{R})_{d} \end{pmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, glycoconjugate.

FIG. 30X

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CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
 - 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 30Y

Insect cell expressed interferon alpha-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 30Z

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E. coli expressed interferon alpha-mucin fusion protein.

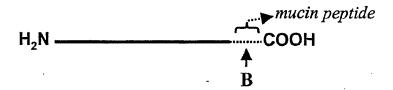
a-e = 0.

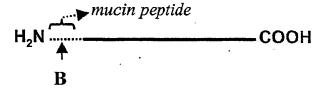
- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 30AA

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{pmatrix}_{e}$$

$$\mathbf{C} \leftarrow (\mathbf{R'})_{\mathbf{n}}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 30BB

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E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 30CC

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 30DD

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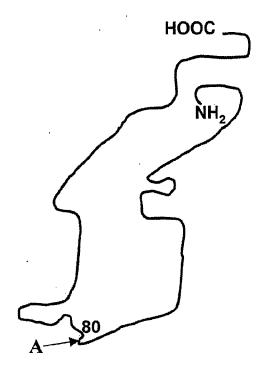
E. coli expressed Interferon alpha (no fusion). a-e, n = 0.

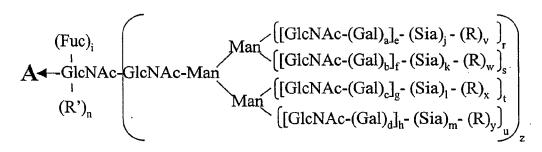
- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, transferrin

a-e=0; n=1; R' = linker-transferrin.

FIG. 30EE

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a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer

FIG. 31A

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CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3: a-g, j-m, i (independently selected) = 0 or 1: r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.

1. Sialidase

2. CMP-SA-PEG, ST3Gal3

```
h = 1 \text{ to } 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 31B

```
Insect cell expressed IF-beta
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3, buffer, salt

b, d, f, h, k, m, n, s, u, w, y = 0; a, c, e, g, i, r, t (independently selected) = 0 or 1; j, l, v, x (independently selected) = 0 or 1: z = 1; R = PEG.

FIG. 31C

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Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

```
a-m, r-z=0; n=1; R'=-Gal-Sia-PEG.
```

FIG. 31D

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 31E

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Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 31F

Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

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NSO expressed IF-beta a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

> CMP-SA-levulinate, ST3Gal3, buffer, salt
> H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 31H

CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.

1. CMP-SA-PEG, α 2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.

FIG. 311

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CHO, BHK, 293 cells, Vero expressed IF-beta a-g, j-m, r-u (independently selected) = 0 or 1; h = 1 to 3; n, v-y = 0; z = 1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 31J

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n=0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 31K

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```
NSO expressed Ifn-beta.

a-d, i-m, r-u, z (independently selected) = 0 or 1;

e-h = 1; n, v-y = 0;

Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal

3. CMP-SA-PEG, ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1;

e-h = 1; R = PEG

n = 0; v-y (independently selected) = 1,

when j-m (independently selected) is 1;
```

FIG. 31L

```
CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 31M

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CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H_4N_2 -PEG

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 31N

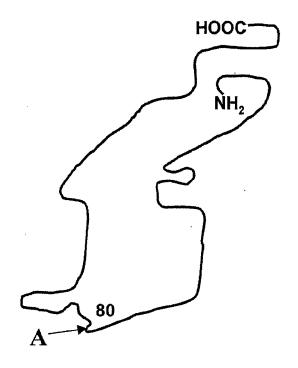
```
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.
```

1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; n, v-y (independently selected) = 0.

FIG. 310

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & & \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-Man} & & & & \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \end{bmatrix}_{s} \\ \operatorname{Man} = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{l} - (\operatorname{R})_{v} \\ (\operatorname{R'})_{n} & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \operatorname{GlcNAc-(Gal)}_{d} = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{b})_{l} - (\operatorname{Sia})_{l} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \operatorname{GlcNAc-(Gal)}_{d} = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{b})_{l} - (\operatorname{Sia})_{l} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l} - (\operatorname{Sia})_{m} - (\operatorname{R})_{v} \end{bmatrix}_{u} \\ \operatorname{GlcNAc-(Gal)}_{d} = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{b})_{l} - (\operatorname{Sia})_{l} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{l} - (\operatorname{Sia})_{m} - (\operatorname{R})_{v} \end{bmatrix}_{u}$$

a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group; R' = H, glycosyl group, modifying group, glycoconjugate.

FIG. 31P

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```
Insect cell expressed Ifn-beta.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 31Q

```
Yeast expressed Ifn-beta.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 31R

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CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- CMP-SA-linker-SA-CMP, ST3Gal3
 ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

```
a-m, q-u (independently selected) = 0 or 1;

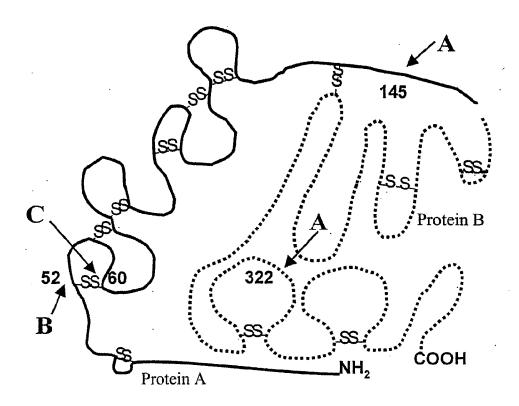
p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 31S

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e} - \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f} - \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g} - \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h} - \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\$$

$$\mathbf{B} \blacktriangleleft \left(\mathsf{Glc}\text{-}(\mathsf{Xyl})_{\mathsf{n}} \right)_{\mathsf{o}}$$

a-d, i, q-u (independently selected) = 0 or 1. o, p (independently selected) = 0 or 1. e-h, n (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-y = 0; R = modifying group, mannose, oligo-

mannose, Sia-Lewis X, Sia-Lewis A..

FIG. 32A

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BHK expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

- 1. Sialidase
 - 2. CMP-SA-PEG (16 mole eq), ST3Gal3

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;

r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;

v, x, (independently selected) = 1,

when j, l (respectively, independently selected) is 1;

R = PEG.
```

FIG. 32B

CHO, BHK, 293 cells, Vero expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y=0; n=0-4.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mole eq), ST3Gal3
- 3. CMP-SA (8 mol eq), ST3Gal3

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v or x, (independently selected) = 1,
when j or l, (respectively, independently selected) is 1;
R = PEG.
```

FIG. 32C

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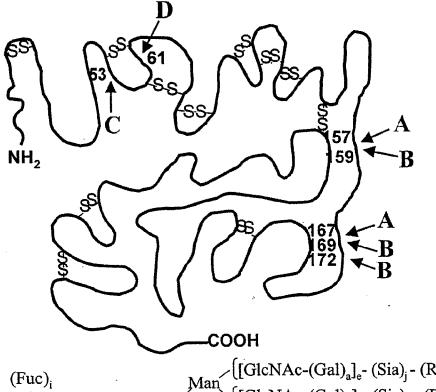
```
NSO expressed Factor VII or VIIa
a--u (independently selected) = 0 or 1;
v-y = 0; n = 0-4;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, o-u (independently selected) = 0 or 1;
n = 0-4; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
Sia = Sia; R = PEG.
```

FIG. 32D

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$$(Fuc)_{i} \qquad \qquad ([GlcNAc-(Gal)_{a}]_{e}-(Sia)_{j}-(R)_{v})_{r} \\ ([GlcNAc-(Gal)_{b}]_{f}-(Sia)_{k}-(R)_{w})_{s} \\ ([GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x})_{t} \\ ([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u} \\ (GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u} \\ (GlcNAc-(Gal)_{d})_{h}-(Sia)_{m}-(R)_{y})_{u} \\ (GlcNAc-(Gal)_{d})_{u}-(R)$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (\operatorname{R})_{z} \end{bmatrix}_{q} \qquad \mathbf{C} \leftarrow \begin{bmatrix} -\operatorname{Glc-(Xyl)}_{aa} \end{bmatrix}_{bb}$$

$$\mathbf{D} \leftarrow \text{-Fuc}\left\{-(\text{GlcNAc})_{\text{cc}} - (\text{Gal})_{\text{dd}} - (\text{Sia})_{\text{ee}}\right\}_{\text{ff}} - (R)_{\text{gg}}$$

a-d, i, n-u (independently selected) = 0 or 1.
bb, cc, dd, ee, ff, gg (independently selected) = 0 or 1.
e-h, aa (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.

FIG. 33A

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```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;

aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)

= 0 or 1;

o, p, z = 0;

j-m, ee, v-y, gg (independently selected) = 0 or 1;

R = PEG.
```

FIG. 33B

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3
- 3. ST3Gal1, CMP-SA

```
a-d, n, p, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
o, z = 0; R = PEG.
```

FIG. 33C

100/498

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1; R = PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when p = 1, z = 1.
```

FIG. 33D

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1; R = PEG;
o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1.
```

FIG. 33E

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```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

1. CMP-SA-levulinate, ST3Gal3, buffer, salt

2. H₄N₂-PEG

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z = 0; R = PEG;
j-m, ee, v-y, gg (independently selected) = 0 or 1.
```

FIG. 33F

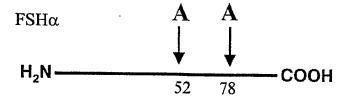
```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

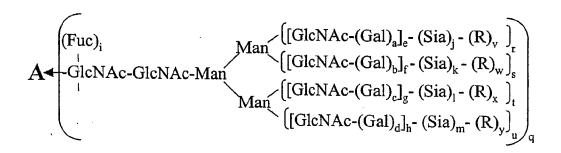
1. CMP-SA-PEG, α2,8-ST

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z = 0; R= PEG;
j-m, ee (independently selected) = 0 to 2;
v-y, gg (independently selected) = 1, when j-m (independently selected) is 2;
```

FIG. 33G

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a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose.

FIG. 34A

103/498

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 34B

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34C

104/498

NSO expressed FSH.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 34D

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34E

105/498

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
 - 2. H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34F

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 34G

106/498

```
Insect cell expressed FSH.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 34H

```
Yeast expressed FSH.

a-m=0; q-y (independently selected) = 0 to 1;

p=1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 341

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CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;

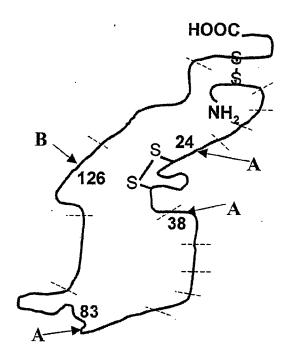
p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-CG.
```

FIG. 34J

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(Fuc)_i

A -GlcNAc-GlcNAc-Man

$$\begin{bmatrix}
[GlcNAc-(Gal)_a]_e - (Sia)_j - (R)_v \\
[GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w \\
Man
\begin{bmatrix}
[GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w \\
Man
\end{bmatrix}_t \\
[[GlcNAc-(Gal)_c]_g - (Sia)_l - (R)_x \\
[[GlcNAc-(Gal)_d]_h - (Sia)_m - (R)_y \\
u
\end{bmatrix}_u$$

B -GalNAc-(Gal)_n-(Sia)_p- (R)_z
_q

a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

v-z = 0;

R = polymer.

FIG. 35A

109/498

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to1; v-z = 0
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 35B

```
Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
b, d, f, h, k, m-q, s, u, w, y, z = 0;
a, c, e, g, i, r, t (independently selected)= 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35C

110/498

```
CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.
```

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 35D

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 35E

111/498

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a-c, e-g, i, r-t, v-x (independently selected) = 0 or 1; d, h, j-q, u, y, z = 0; R = PEG.

FIG. 35F

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 35G

112/498

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc-PEG

e, i, r, v (independently selected) = 0 or 1; a-h, j-q, s-u, w-z = 0; R = PEG.

FIG. 35H

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT-1, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a, e, i, r, v (independently selected) = 0 or 1; b-d, f-h, j-q, s-u, w-z = 0; R = PEG.

FIG. 351

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Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT-1, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

a, e, i, j, r, v (independently selected) = 0 or 1; b-d, f-h, k-q, s-u, w-z = 0; R = PEG.

FIG. 35J

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

a-c, e-g, i-l, r-t, v-x (independently selected) = 0 or 1; d, h, m-q, u, y, z = 0; R = PEG.

FIG. 35K

114/498

```
Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. α2,6-sialyltransferase, CMP-SA-PEG

```
a-c, e-g, i-l, r-t, v-x (independently selected)
= 0 or 1;
d, h, m-q, u, y, z = 0; R = PEG.
```

FIG. 35L

```
CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z=0.
```

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 3. CMP-SA-PEG, ST3Gal1

```
a-h, q, i-o, r-u (independently selected)
= 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 35M

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CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, q-u (independently selected) = 0 or 1; v-y = 0; p, z = 0 or 1; R = PEG.

FIG. 35N

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, α 2,8-sialyltransferase

a-h, i-o, q-u (independently selected) = 0 or 1; v-y=0; p, z=0 or 1; R=SA-PEG.

FIG. 350

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CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, α 2,8-sialyltransferase

a-h, i-o, p-u, v-z (independently selected) = 0 or 1; R = SA-PEG.

FIG. 35P

yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; a-m, n-q, s, w, z = 0; $R = (Man)_n$ where n = 1-5, linear or branched.

- 1. mannosidases
- 2. GNT-1, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal
- 4. ST3Gal3, CMP-SA-PEG

a, e, j, r, v (independently selected) = 0 or 1; b-d, f-i, k-q, s-u, w-z = 0; R = PEG.

FIG. 35Q

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```
yeast or fungi expressed EPO

r, t, u, v, x, y (independently selected) = 0 or 1;

a-m, n-q, s, w, z = 0; R = (Man)<sub>n</sub>

where n = 1-5, linear or branched.
```

- 1. mannosidases
- 2. GNT-1, UDP-GlcNAc-PEG

e, r, v (independently selected) = 0 or 1; a-h, i-q, s-u, w-z = 0; R = PEG.

FIG. 35R

```
yeast or fungi expressed EPO

r, t, u, v, x, y (independently selected) = 0 or 1;

a-m, n-q, s, w, z = 0; R = (Man)_n

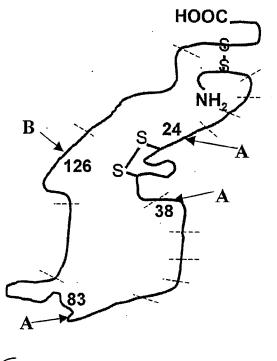
where n = 1-5, linear or branched.
```

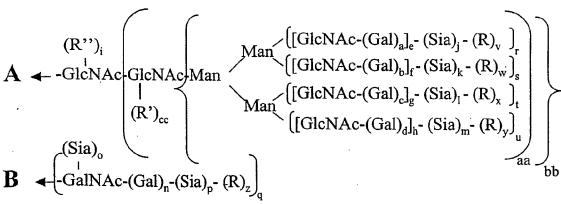
- 1. mannosidase-I
- 2. GNT-1, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal
- 4. ST3Gal3, CMP-SA-PEG

```
a, e, j, r, t-u, v, x, y (independently selected)
= 0 or 1;
b-d, f-i, k-q, s, w, z = 0;
(R)<sub>v</sub> = PEG; (R)<sub>x</sub> and (R)<sub>y</sub> = Man.
```

FIG. 35S

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a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; aa, bb = 1; cc = 0; R = polymer; R" and R' = sugar-polymer or Fuc.

FIG. 35T

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```
yeast or fungi expressed EPO
r, t, u, v, x, y (independently selected) = 0 or 1;
cc, a-m, n-q, s, w, z = 0;
aa, bb = 1;
R = (Man), where n = 1-100, linear or branched.
```

- 1. endo-H
- 2. galactosyltransferase, UDP-Gal-PEG

```
i (independently selected) = 0 or 1;
aa, bb, cc, a-h, j-z = 0; R" = Gal-PEG.
```

FIG. 35U

```
yeast or fungi expressed EPO

r, t, u, v, x, y (independently selected) = 0 or 1;

cc, a-m, n-q, s, w, z = 0; aa, bb = 1;

R = (Man)_n where n = 1-100, linear or branched.
```

- 1. endo-H
- 2. galactosyltransferase, UDP-Gal
- · ▼ 3. ST3Gal3, CMP-SA-PEG

i (independently selected) = 0 or 1; aa, bb, cc, a-h, j-z = 0; R" = Gal-SA-PEG.

FIG. 35V

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```
Insect cell expressed EPO

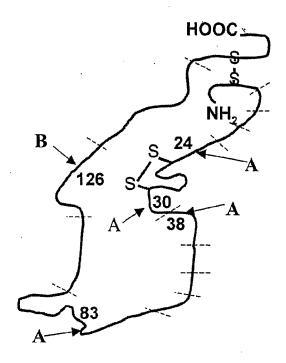
a-d, f, h, j-m, n-q, s, u, v-z = 0;
e, g, i, r, t (independently selected) = 0 or 1;
aa = 1; R" = Fuc.
```

- 1. mannosidases
- 2. galactosyltransferase, UDP-Gal-PEG

```
cc, e, i, r, v (independently selected) = 0 or 1;
bb, a-h, j-q, s-u, w-z = 0; aa = 1; R' = Gal-PEG.
```

FIG. 35W

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$$(Fuc)_{i}$$

$$A \leftarrow -GlcNAc-GlcNAc-Man$$

$$(GlcNAc-(Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v}$$

$$[GlcNAc-(Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w}$$

$$[GlcNAc-(Gal)_{b}]_{g} - (Sia)_{l} - (R)_{v}$$

$$[GlcNAc-(Gal)_{b}]_{g} - (Sia)_{l} - (R)_{v}$$

$$[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

$$[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

$$[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

$$[GlcNAc-(Gal)_{b}]_{g} - (Sia)_{l} - (R)_{v}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer.

FIG. 35X

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```
NSO expressed NESP
q = 1; a-i, n, r-u (independently selected) = 0
or 1; j-m, o, p, v-z = 0

1. CMP-SA-levulinate, ST3Gal3,
buffer, salt
2. H<sub>4</sub>N<sub>2</sub>-PEG

q = 1; a-i, j-n, r-y (independently selected) =
0 or 1;
o, p, z = 0; R = PEG.
```

FIG. 35Y

```
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, α 2,8-ST

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m (independently selected) = 0 to 2;

v-y (independently selected) = 1,

when j-m (independently selected) is 2;

R = PEG; z = 0.
```

FIG. 35Z

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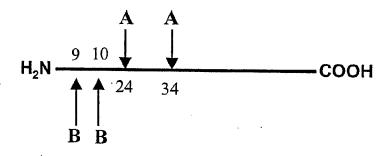
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0

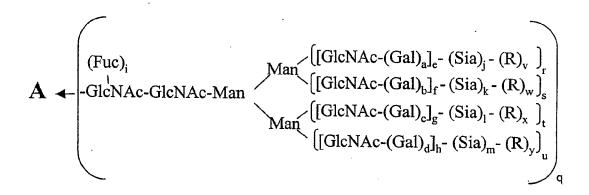
1 CMP-SA, poly- α 2,8-ST

a-g, n, q = 1; h = 1 to 3; i, j-m, o, p, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-40; R = Sia.

FIG. 35AA

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{bmatrix}_{aa}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 36A

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CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h=1; v-z=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 36B

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3 & ST3Gal1

a-d, i-m, p-u, aa (independently selected) = 0 or 1;
o, z = 0; n, e-h = 1;
v-y (independently selected) = 0 or 1; R = PEG.

FIG. 36C

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NSO expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-PEG, ST3Gal1

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1; n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.

FIG. 36D

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-y, as (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; R = PEG.

FIG. 36E

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CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h=1; v-z=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-d, i-m, o-y, as (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = PEG.

FIG. 36F

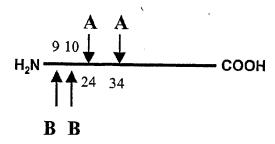
CHO, BHK, 293 cells, Vero expressed GMCSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

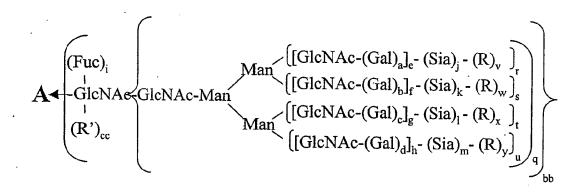
1. CMP-SA, α2,8-ST

a-d, i, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; j-m (independently selected) = 0-20; v-z (independently selected) = 0.

FIG. 36G

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{pmatrix}_{aa}$$

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group. glycoconjugate.

FIG. 36H

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```
Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, n, q-u (independently selected) = 0 or 1;

j-m = 0; v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 361

```
Yeast expressed GM-CSF.

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1;

bb = 1; R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

- 1. Endoglycanase
- 2. mannosidase (if aa = 1).
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.
```

FIG. 36J

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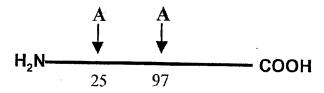
CHO, BHK, 293 cells, Vero expressed GM-CSF. a--m, o-u, aa, bb (independently selected) = 0 or 1; n, v-z, cc = 0.

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-linker-SA-CMP, ST3Gal1
- 3. ST3Gal3, transferrin

a--m, p-u, z, as (independently selected) = 0 or 1; o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 36K

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \\ [\mathrm{GlcNAc\text{-}(Gal)}_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ [\mathrm{GlcNAc\text{-}(Gal)}_b]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc\text{-}(Gal)}_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u = \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_b]_f - (\mathrm{Sia})_l - (\mathrm{R})_x \\ [\mathrm{GlcNAc\text{-}(Gal)}_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u = \mathbf{A}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 37A

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```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

1. Sialidase

2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37B

```
CHO, BHK, 293 cells, Vero expressed IF-gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37C

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```
NSO expressed Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37D

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37E

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```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3,
2. H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37F

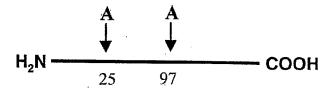
```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 37G

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-Man} \\ (R')_{n} \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{a}]_{e} - (\operatorname{Sia})_{j} - (R)_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{k} - (R)_{w} \end{bmatrix}_{s} \\ (\operatorname{GlcNAc-(Gal)}_{c}]_{g} - (\operatorname{Sia})_{l} - (R)_{x} \end{bmatrix}_{t} \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \end{bmatrix}_{u} = 0$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 37H

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```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;

j-m = 0; v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 371

```
Yeast expressed IF-gamma.

a-m=0; q-y (independently selected) = 0 to 1; p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 37J

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CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase.

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 37K

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.
```

1. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1;
n, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37L

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```
Insect or fungi cell expressed IF-gamma.

a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.
```

FIG. 37M

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

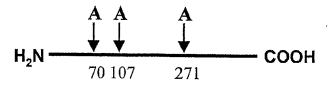
1. CMP-SA-PEG, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1;
```

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
when j-m (independently selected) = 2;
R = PEG.
```

FIG. 37N

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \right]_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{u} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{u} \\ \left[\operatorname{GlcNAc-(Ga$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 38A

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```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub> antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 38B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub> antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38C

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```
CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub>-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

1. CMP-SA-levulinate, ST3Gal3, buffer, salt

 $2. H_4 N_2$ -PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38E

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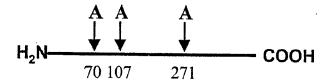
CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 38F

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e} - \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f} - \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g} - \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h} - \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right]_{u} \\ q \\ p \\ \end{bmatrix}$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 38G

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Insect or fungi cell expressed α_1 -antitrypsin. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1; j-m = 0; v-y (independently selected) = 1, when e-h (independently selected) is 1; R = PEG.

FIG. 38H

Yeast expressed α_1 -antitrypsin. a-m=0; q-y (independently selected) = 0 to 1; p=1; R (branched or linear) = Man, oligomannose.

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 381

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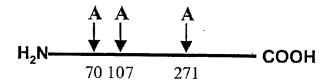
CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

```
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.
```

FIG. 38J

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$$(Fuc)_{i}$$

$$A \leftarrow GlcNAc - GlcNAc - Man$$

$$(R')_{p}$$

$$(Fuc)_{i}$$

$$(GlcNAc - (Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v}$$

$$[GlcNAc - (Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w}$$

$$[GlcNAc - (Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x}$$

$$[GlcNAc - (Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x}$$

$$[GlcNAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R', R" (independently selected) = sugar, glycoconjugate.

FIG. 38K

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Yeast expressed alpha-1 antitrypsin.
a-h, i-m, p, q = 0;
R (independently selected) = mannose, oligomannose, polymannose;
r-u, v-y (independently selected) = 0 or 1; n, o = 1.

- 1. endoglycanase
- ↓ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

FIG. 38L

```
Plant expressed alpha-1 antitrypsin.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n=1; R' = xylose
```

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

FIG. 38M

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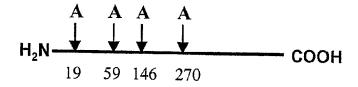
CHO, BHK, 293 cells, Vero, transgenic animal expressed α_1 antitrypsin. a-h, i-o, r-u (independently selected) = 0 or 1; p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 38N

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{a}]_{e}^{-} & (\mathrm{Sia})_{j}^{-} & (\mathrm{R})_{v} \end{bmatrix}_{r}^{r} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{b}]_{f}^{-} & (\mathrm{Sia})_{k}^{-} & (\mathrm{R})_{w} \end{bmatrix}_{s}^{r} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{c}]_{g}^{-} & (\mathrm{Sia})_{l}^{-} & (\mathrm{R})_{x} \end{bmatrix}_{t}^{r} \\ [\mathrm{GlcNAc\text{-}}(\mathrm{Gal})_{d}]_{h}^{-} & (\mathrm{Sia})_{m}^{-} & (\mathrm{R})_{y} \end{bmatrix}_{u}^{q}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 39A

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CHO, BHK, 293 cells, Vero expressed Cerezyme a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 39B

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-M-6-P (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = mannose-6-phosphate
```

FIG. 39C

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```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate
```

FIG. 39D

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- CMP-SA-levulinate, ST3Gal3, buffer, salt
 H N. spacer M & P. and J. A.
- ↓ 2. H₄N₂-spacer-M-6-P or clustered M-6-P

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = M-6-P or clustered M-6-P
```

FIG. 39E

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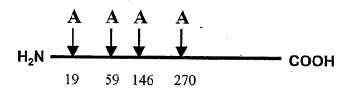
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 39F

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e} - \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f} - \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g} - \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h} - \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ p$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG: 39G

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```
Insect cell expressed Cerezyme.

a-d, f, h, j-m, s, u, v-y = 0;

e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;

j-m = 0;

v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 39H

```
Yeast expressed Cerezyme.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 391

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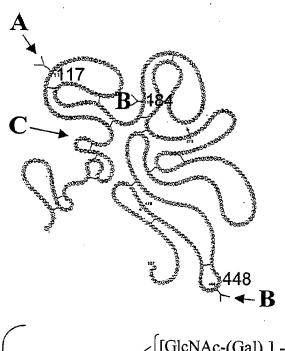
```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

```
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0; v-y (independently selected) = 0 or 1;
R = linker-transferrin.
```

FIG. 39J

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$$(Fuc)_{i}$$

$$\mathbf{B} \leftarrow GlcNAc - GlcNAc - Man$$

$$[[GlcNAc - (Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v}]_{r}$$

$$[[GlcNAc - (Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w}]_{s}$$

$$[[GlcNAc - (Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x}]_{t}$$

$$[[GlcNAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}]_{u}$$

$$\mathbf{C} \leftarrow -(\operatorname{Fuc})_{0-1}$$
 $\mathbf{A} \leftarrow -\operatorname{GlcNAc-GlcNAc-Man}$
 $\operatorname{Man} - [\operatorname{Man}]_{0-12}$
 $\operatorname{Man} - [\operatorname{Man}]_{0-6}$
 $\operatorname{Man} - [\operatorname{Man}]_{0-6}$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40A

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```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; o, v-y = 0.
```

- 1. Mannosidase(s), sialidase
- 2. GNT1,2 (4 and/or 5) UDP-GlcNAc
- 3. Gal transferase, UDP-Gal
- 4. CMP-SA-PEG, ST3Gal3

```
A = B; a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1;
o = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG
```

FIG. 40B

```
Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

```
A = B; b, d, f, h, k, m, o, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
n = 1; j, l, v, x (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40C

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Yeast expressed tPA B = A; i = 0.

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

$$A = B$$
; a-n, r-y = 0; $o = 1$; R' = Gal-PEG.

FIG. 40D

Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. alpha and beta mannosidases
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 40E

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Insect or fungi cell expressed tPA

A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; b, d, f, h, j-o, s, u, w, y = 0; a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1; n = 1; R = PEG.

FIG. 40F

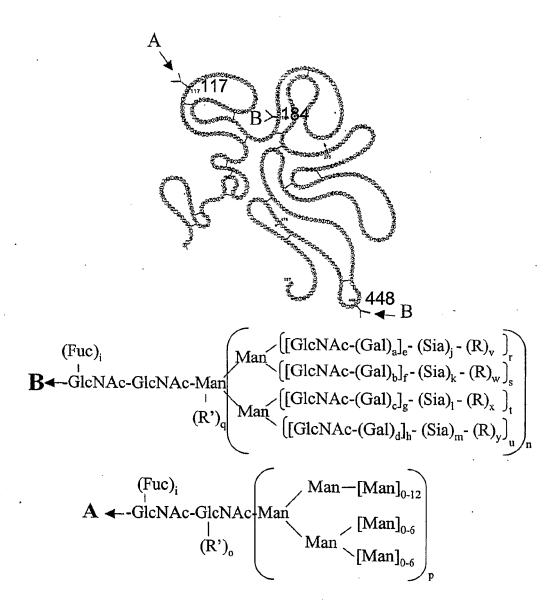
Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1 & 2, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

A = B; b, d, f, h, j-o, s, u, w, y = 0; a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1; n = 1; R = PEG.

FIG. 40G

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a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40H

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```
NSO expressed tPA
A = B; a-m, r-u (independently selected) = 0 or 1;
n = 1; o, p, q, v-y = 0
```

```
    sialidase, alpha-galactosidase
    CMP-SA-levulinate, ST3Gal3,
    H<sub>4</sub>N<sub>2</sub>-PEG
```

```
A = B; a-m, r-y (independently selected) = 0 or 1;

n = 1; o, p, q = 0;

v-y (independently selected) = 1,

when j-m (independently selected) is 1;

R = PEG.
```

FIG. 401

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n, p = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; q, o, v-y = 0.
```

- 1. alpha and beta Mannosidases
- 2. CMP-SA, ST3Gal3
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1; o = 1;
q, p, v-y = 0; j-m (independently selected) = 0 or 1;
R' = Gal-PEG
```

FIG. 40J

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```
Plant expressed tPA

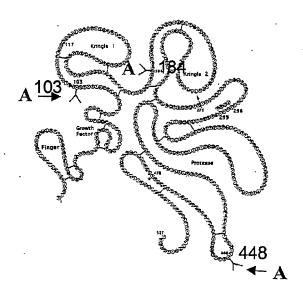
A = B; a-d, f, h, j- m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n = 1; R' = xylose
```

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
A = B; a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

FIG. 40K

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \right]_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left[\operatorname{Gia}_{h^{-}} \left(\operatorname{Sia}_{h^{-}} \left(\operatorname{Sia}_$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 40L

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CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 40M

```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40N

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```
NSO expressed TNK tPA

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

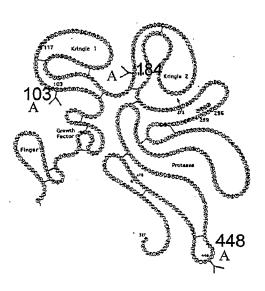
Sia (independently selected) = Sia or Gal.
```

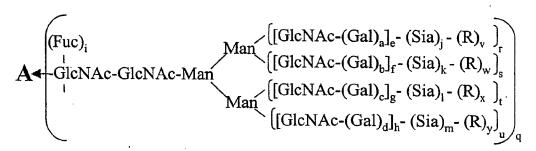
- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 400

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a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

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CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40Q

```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 40R

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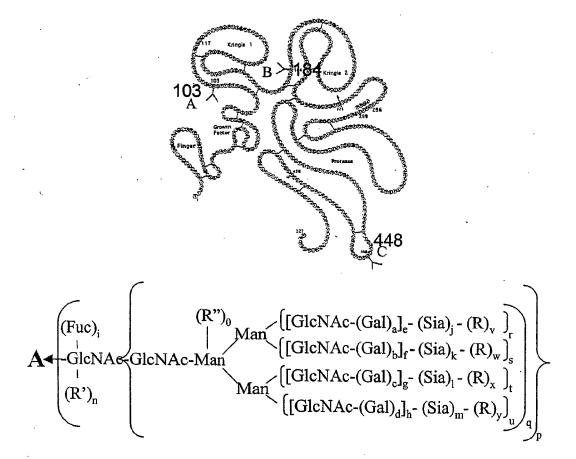
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 40S

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a-d, i, n-y (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

R" = glycosyl residue.

FIG. 40T

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```
Insect cell expressed TNK tPA
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;

j-m = 0; v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 40U

```
Yeast expressed TNK tPA a-m=0; q-y (independently selected) = 0 to 1; p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-PEG.
```

FIG. 40V

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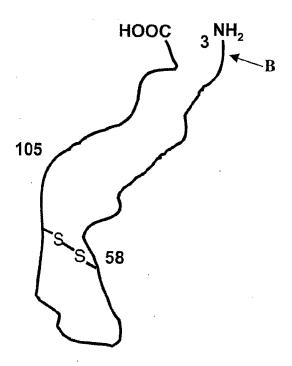
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, anti-TNF IG chimera produced in CHO.

a-m, r-u (independently selected) = 0 or 1; p, q = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-anti-TNF IG chimera protein.

FIG. 40W

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc} - (\mathrm{Gal})_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose.

FIG. 41A

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CHO, BHK, 293 cells, Vero expressed IL-2 a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 41B

Insect cell expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 41C

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E. coli expressed IL-2 a-e = 0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 41D

NSO expressed IL-2

a, e (independently selected) = 0 or 1;

b, c, d = 0

- 1. CMP-SA-levulinate, ST3Gal1
- 2. H₄N₂-PEG

a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

FIG. 41E

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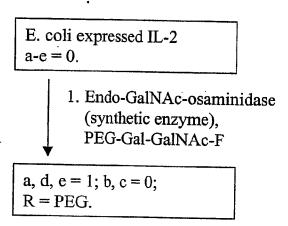


FIG. 41F

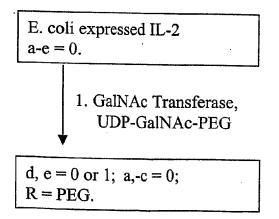


FIG. 41G

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2 peptides

A and A' - N-linked sites

B - O-linked sites

$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} & ([\operatorname{GlcNAc-(Gal})_{a}]_{e^{-}} & (\operatorname{Sia})_{j^{-}} & (\operatorname{R})_{v} \\ \operatorname{GlcNAc-GlcNAc-Man} & ([\operatorname{GlcNAc-(Gal})_{b}]_{f^{-}} & (\operatorname{Sia})_{k^{-}} & (\operatorname{R})_{w} \\ \operatorname{Man} & ([\operatorname{GlcNAc-(Gal})_{c}]_{g^{-}} & (\operatorname{Sia})_{l^{-}} & (\operatorname{R})_{x} \\ & ([\operatorname{GlcNAc-(Gal})_{d}]_{h^{-}} & (\operatorname{Sia})_{m^{-}} & (\operatorname{R})_{y} \end{bmatrix}_{u} \end{bmatrix}_{aa}$$

$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{pmatrix}$$

a-d, i, n-u (independently selected) = 0 or 1. aa, bb (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer, glycoconjugate.

FIG. 42A

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CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.

- 1. Sialidase
 - 2. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1;
o, p, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42B

CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3
- 3. ST3Gal1, CMP-SA

e-h = 1 to 4; aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1; o, z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 42C

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CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;

v-z = 0.

1. CMP-SA-PEG, ST3Gal3

e-h = 1 to 4; aa, bb, a-d, i, n-u (independently selected) = 0 or 1; z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 42D

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;
v-z = 0.

1. CMP-SA-PEG, ST3Gal1

e-h = 1 to 4; aa, bb, a-d, i, n-u (independently selected) = 0 or 1; z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 42E

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.
```

1. CMP-SA-PEG, α 2,8-ST

```
e-h = 1 to 4;
aa, bb, a-d, i, n-y (independently selected) = 0 or 1;
z = 0; j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG.
```

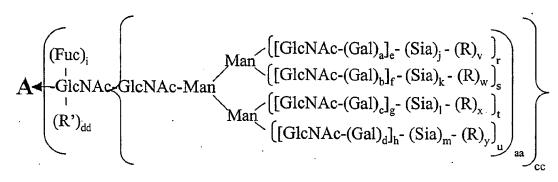
FIG. 42F

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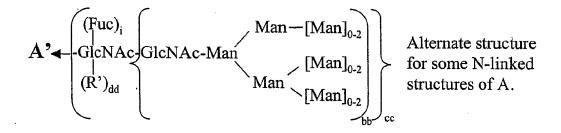
2 peptides

A or A' - N-linked sites

B - O-linked sites



$$\mathbf{B} \quad \bullet \begin{pmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{pmatrix}_{q}$$



a-d, i, n-u, (independently selected) = 0 or 1. aa, bb, cc, dd (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0; R = modifying group, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 42G

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

1. CMP-SA-levulinate, ST3Gal3,2. H₄N₂-PEG

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1;
dd, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42H

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

1. endo-H2. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z=0; R'=-Gal-PEG.
```

FIG. 421

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

- 1. ST3Gal3, CMP-SA
- 2. endo-H
- 3. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

FIG. 42J

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- $3.\ galactosyltransferase,\ UDP\mbox{-}Gal\mbox{-}PEG$

```
e-h = 1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0; R = PEG.
```

FIG. 42K

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

1. mannosidases
2. GNT-1,2, 4 & 5; UDP-GlcNAc
```

2. GN1-1,2, 4 & 5; UDP-GICNAC
3. galactosyltransferase, UDP-Gal
4. ST3Gal3, CMP-SA

e-h = 1 to 4; aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;

FIG. 42L

dd, v-z = 0.

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

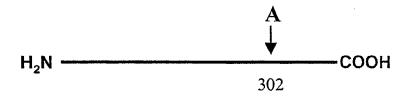
dd, v-z = 0.
```

1. mannosidases2. GNT-1, UDP-GlcNAc-PEG

```
e-h = 0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0.
```

FIG. 42M

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc\text{-}(Gal)}_{a}]_{e}^{-} & (\mathrm{Sia})_{j}^{-} & (\mathrm{R})_{v} \end{bmatrix}_{r}^{r} \\ [\mathrm{GlcNAc\text{-}Gal)}_{b}]_{f}^{-} & (\mathrm{Sia})_{j}^{-} & (\mathrm{R})_{v} \end{bmatrix}_{r}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{b}]_{f}^{-} & (\mathrm{Sia})_{k}^{-} & (\mathrm{R})_{w} \end{bmatrix}_{s}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{c}]_{g}^{-} & (\mathrm{Sia})_{l}^{-} & (\mathrm{R})_{x} \end{bmatrix}_{t}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{d}]_{h}^{-} & (\mathrm{Sia})_{m}^{-} & (\mathrm{R})_{y} \end{bmatrix}_{u}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{d}]_{h}^{-} & (\mathrm{Sia})_{m}^{-} & (\mathrm{R})_{w} \end{bmatrix}_{u}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{d}]_{u}^{-} & (\mathrm{Sia})_{m}^{-} & (\mathrm{R})_{w} \end{bmatrix}_{u}^{r} \\ [\mathrm{GlcNAc\text{-}(Gal)}_{d}]_{u}^{-} & (\mathrm{R})_{w} \\ [\mathrm{GlcNAc\text{-}(Ga$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 43A

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CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 43B

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 43C

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CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 43D

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
 - 2. H₄N₂-PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 43E

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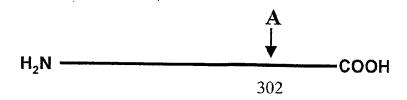
```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

1. CMP-SA, α2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 43F

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e} - \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f} - \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \end{bmatrix}_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{g} - \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h} - \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right]_{u} \\ q \\ p \\ \end{bmatrix}$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 43G

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```
Insect cell expressed Urokinase.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 43H

```
Yeast expressed Urokinase.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 431

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```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated Urokinase produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-Urokinase.
```

FIG. 43J

```
Isolated Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0; n = 0;

Sia (independently selected) = Sia or SO<sub>4</sub>;

Gal (independently selected) = Gal or GalNAc;

GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

- 1. sulfohydrolase
- 2. CMP-SA-PEG, sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
n = 0; e-h = 1; Sia = Sia;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 43K

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```
Isolated Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; n = 0; v-y = 0;

Sia (independently selected) = Sia or SO<sub>4</sub>;

Gal (independently selected) = Gal or GalNAc;

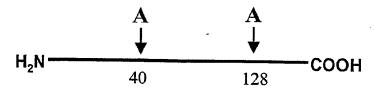
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

- 1. sulfohydrolase, hexosaminidase
- 2. UDP-Gal-PEG, galactosyltransferase

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-n = 0; Gal (independently selected) = Gal;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 43L

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$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j^{-}} \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k^{-}} \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l^{-}} \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y=0; R = polymer, glycoconjugate.

FIG. 44A

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```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 44B

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 44C

194/498

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 44D

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 44E

195/498

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 44F

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ -\operatorname{GlcNAc-Man} \\ (\operatorname{R'})_{n} \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_{a}]_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \end{bmatrix}_{s} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \end{bmatrix}_{t} \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} = 0$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 44G

197/498

```
Insect cell expressed DNase I.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1; j-n = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 44H

```
Yeast expressed DNase I.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-n, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 441

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CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;

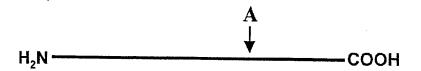
p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker- alpha-1-Proteinase inhibitor.
```

FIG. 44J

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$$(Fuc)_{i}$$

$$A \leftarrow GlcNAc-GlcNAc-GlcNAc-Man$$

$$(R')_{n}$$

$$(R')_{n}$$

$$(Fuc)_{i}$$

$$(GlcNAc-(Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v}$$

$$[GlcNAc-(Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w}]_{s}$$

$$[[GlcNAc-(Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x}]_{t}$$

$$[[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}]_{u}$$

$$[[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}]_{u}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 45A

200/498

```
CHO, BHK, 293 cells, Vero expressed Insulin. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 45B

```
Insect cell expressed Insulin.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 45C

201/498

Yeast expressed Insulin.

a-n = 0; r-y (independently selected) = 0 to 1; z = 1;

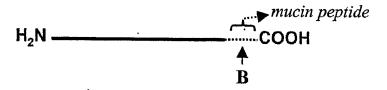
R (branched or linear) = Man, oligomannose or polysaccharide.

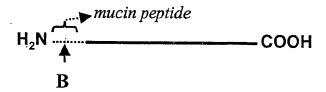
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

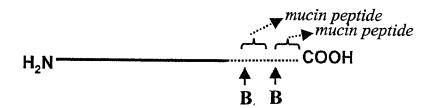
a-m, r-z=0; n = 1; R' = -Gal-PEG.

FIG. 45D

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{pmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 45E

203/498

CHO, BHK, 293 cells, Vero expressed insulinmucin fusion protein.

a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 45F

Insect cell expressed Insulin-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 45G

204/498

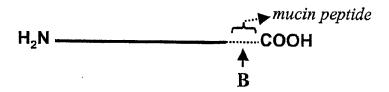
E. coli expressed Insulin-mucin fusion protein. a-e = 0.

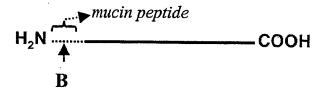
- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

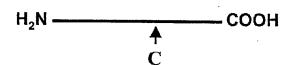
c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 45H

205/498







$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (\operatorname{R})_{d} \end{pmatrix}_{e}$$

$$\mathbb{C} \leftarrow (\mathbb{R}')_n$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligo-mannose.

FIG. 451

206/498

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 45J

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 45K

207/498

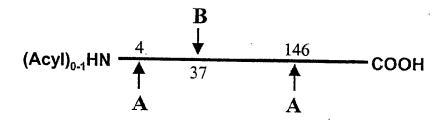
E. coli expressed Insulin (N)—no mucin peptide. a-e, n = 0.

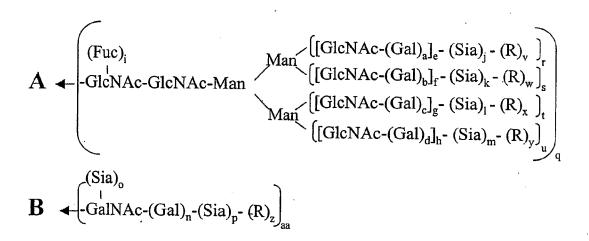
- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

```
a-e = 0; n = 1;
R' = linker-transferrin.
```

FIG. 45L

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a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 46A

209/498

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-linker-lipid-A, ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = linker-lipid-A.
```

FIG. 46B

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. sialidase
- 2. CMP-SA-linker-tetanus toxin, ST3Gal1
- ▼ 3. CMP-SA, ST3Gal3

a-d, i-m, p-u, z, as (independently selected) = 0 or 1; o, v-y=0; n, e-h=1; R = tetanus toxin.

FIG. 46C

210/498

```
NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-KLH, ST3Gal1

```
a-d, i-n, p-u, z, aa (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.
```

FIG. 46D

```
Yeast expressed M-antigen.
a-p, z = 0; q-y, aa (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

α1,2-mannosidase
 GNT 1,
 UDP-GlcNAc-linker-diphtheria toxin.

e, q, l, m, r, t, u, v, aa (independently selected) =0 or 1; a-d, f-h, j, k, n-p, s, w-z = 0; Sia = Man; R = linker-diphtheria toxin.

FIG. 46E

211/498

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. CMP-SA-levulinate, ST3Gal3,
- 2. H₄N₂-linker-DNA

a-d, i-m, o-y, as (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = linker-DNA.

FIG. 46F

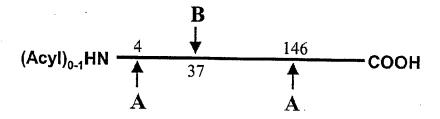
CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-n, o-u, aa (independently selected) = 0 or 1; e-h=1; v-z=0.

1. CMP-SA, poly- α 2,8-ST

a-d, i, n-u, aa (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-100; v-z (independently selected) = 0.

FIG. 46G

212/498



$$\mathbf{A} \leftarrow (\operatorname{Fuc})_{i} \\ -\operatorname{GlcNAc-GlcNAc-Man} \\ | (\operatorname{R'})_{cc} \\ | (\operatorname{R'})_{cc} \\ | (\operatorname{GlcNAc-(Gal)}_{a}]_{e^{-}} (\operatorname{Sia})_{j^{-}} (\operatorname{R})_{v} \\ | (\operatorname{GlcNAc-(Gal)}_{b}]_{f^{-}} (\operatorname{Sia})_{k^{-}} (\operatorname{R})_{w} \\ | (\operatorname{GlcNAc-(Gal)}_{c}]_{g^{-}} (\operatorname{Sia})_{l^{-}} (\operatorname{R})_{x} \\ | (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ | (\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} (\operatorname{Gal})_{m^{-}} (\operatorname{R})_{y} \\ | (\operatorname{GlcNAc-(Gal)}_{d})_{m^{-}} (\operatorname{Gal})_{m^{-}} (\operatorname$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{bmatrix}_{aa}$$

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-p (independently selected) = 0 to 100. Cc, v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group, glycoconjugate.

FIG. 46H

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```
Insect cell expressed M-antigen.
a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;
bb = 1;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

1. GNT-2, UDP-GlcNAc-linker-Neisseria protein

```
a, c, e, g, i, n, q, r, t, v, x, aa (independently selected) = 0 or 1;
b, d, f, h, j-p, s, u, w, y, z, cc = 0;
bb = 1; R = -linker-Neisseria protein.
```

FIG. 461

```
Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

1. Endoglycanase

2. Galactosyltransferase, UDP-Gal-linker-Neisseria protein

```
a-p, r-z, bb = 0;
q, aa, cc (independently selected) = 0 or 1;
R' = -Gal-linker-Neisseria protein.
```

FIG. 46J

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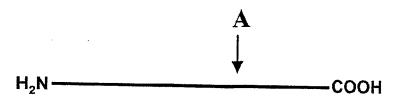
```
Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, as (independently selected) = 0 to 1; bb = 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc3. UDP-Gal, Galactosyltransferase,

```
a, c, e, g, j, l, q, r, t, aa (independently selected) = 0 or 1;
b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.
```

FIG. 46K

215/498



$$(Fuc)_{i} \\ \mathbf{A} \leftarrow GlcNAc - GlcNAc - Man \\ \begin{bmatrix} [GlcNAc - (Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v} \end{bmatrix}_{r} \\ \begin{bmatrix} [GlcNAc - (Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w} \end{bmatrix}_{s} \\ (R')_{n} \\ \end{bmatrix} \\ Man \\ \begin{bmatrix} [GlcNAc - (Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x} \end{bmatrix}_{t} \\ \begin{bmatrix} [GlcNAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y} \end{bmatrix}_{u} \\ \end{bmatrix}_{z}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 47A

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CHO, BHK, 293 cells, Vero expressed Growth Hormone.

```
a-m, r-u (independently selected) = 0 or 1;

n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 47B

```
Insect cell expressed growth hormone.

a-h, j-n, s-y = 0;

i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected)= 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 47C

217/498

Yeast expressed growth hormone.

a-n=0; r-y (independently selected) = 0 to 1; z=1;

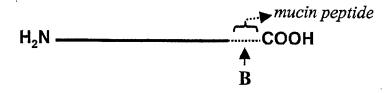
R (branched or linear) = Man, oligomannose or polysaccharide.

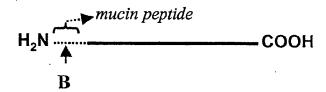
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

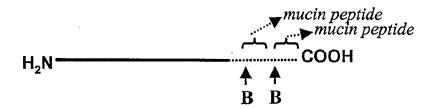
a-m, r-z=0; n = 1; R' = -Gal-PEG.

FIG. 47D

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc} - (\mathrm{Gal})_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose.

FIG. 47E

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CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein.

a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 47F

Insect cell expressed Growth Hormone-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 47G

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E. coli expressed growth hormone-mucin fusion protein.

$$a-e=0$$
.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 47H

E. coli expressed growth hormone-mucin fusion protein.

$$a-e, n = 0.$$

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 471

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E. coli expressed growth hormone-mucin fusion protein.

```
a-e, n = 0.
```

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- ▼ 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 47J

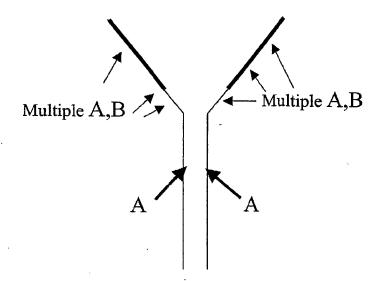
E. coli expressed growth hormone(N)—no mucin peptide.a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R' = linker-transferrin.

FIG. 47K

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ -\operatorname{GlcNAc-Man} & & & \\ (\operatorname{GlcNAc-Gal})_{a} \\ -\operatorname{GlcNAc-Man} & & & \\ (\operatorname{GlcNAc-Gal})_{b} \\ -\operatorname{GlcNAc-Gal})_{b} \\ -\operatorname{GlcNAc-Gal})_{c} \\ \mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{GlcNAc-Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal} \\ -\operatorname{Gal} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{b} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal} \\ -\operatorname{Gal})_{a} \\ -\operatorname{Gal})_$$

a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. n, v-y=0;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

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CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

- 1. CMP-SA, ST3Gal1
- 2. galactosyltransferase, UPD-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48B

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

- 1. sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-i, p-u, z, aa (independently selected) = 0 or 1; n = 1; o, j-m, v-y = 0; R = PEG.

FIG. 48C

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CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48D

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.

a-m, o-u, aa (independently selected) = 0 or 1;

n = 1; v-z = 0.

1. CMP-SA, ST3Gal12. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48E

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CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal1 · · · 2. H₄N₂-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48F

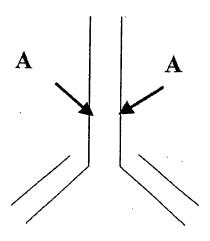
CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. CMP-SA-PEG, α2,8-ST

a-i, o, q-u, v-z, aa (independently selected) = 0 or 1; n = 1; j-m, p (independently selected) = 0 to 2; v-z (independently selected) = 1, when j-m, p (independently selected) is 2; R = PEG.

FIG. 48G

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Fuc)_i
GlcNAc-GlcNAc-Man
$$\begin{bmatrix}
[GlcNAc-(Gal)_a]_e - (Sia)_j - (R)_v \\
[GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w \\
Man
\begin{bmatrix}
[GlcNAc-(Gal)_c]_g - (Sia)_l - (R)_x \\
[GlcNAc-(Gal)_d]_h - (Sia)_m - (R)_y \\
\end{bmatrix}_{u} \\
z \\
q$$

a-d, i, l, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-k (independently selected) = 0 or 1.

M = 0 to 20.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

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```
CHO, BHK, 293 cells, Vero expressed Herceptin.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 51,
when j, l (independently selected) is 1.
```

FIG. 49B

```
CHO, BHK, 293 cells, Vero or fungal expressed Herceptin.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

1. galactosyltransferase, UPD-Gal-Toxin

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

FIG. 49C

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Fungi expressed Herceptin.

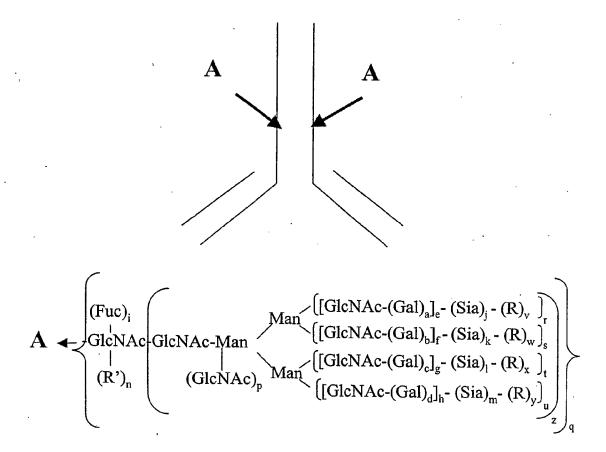
```
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y=0; q, z=1.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 49D

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a-d, i, p-u, (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 50A

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```
CHO, BHK, 293 cells, Vero expressed Synagis.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1;
b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

1. galactosyltransferase, UPD-Gal

```
2. CMP-SA-PEG, ST3Gal3
```

```
a, c, i, j, w, (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 50B

```
CHO, BHK, 293 cells, Vero or fungal expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

1. galactosyltransferase, UPD-Gal-PEG

```
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

FIG. 50C

231/498

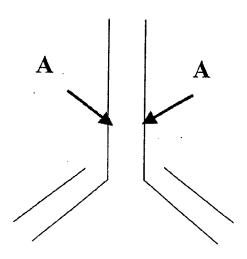
Fungi expressed Synagis. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; q, n=1; R'=-Gal-Sia-PEG.

FIG. 50D

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-\operatorname{Gal}}_{a} \end{bmatrix}_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \end{bmatrix}_{r} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{b} \right]_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \end{bmatrix}_{s} \\ \operatorname{Man} \begin{bmatrix} (\operatorname{GlcNAc-\operatorname{Gal}})_{b} \right]_{f} - (\operatorname{Sia})_{l} - (\operatorname{R})_{w} \end{bmatrix}_{t} \\ \left[(\operatorname{R'})_{n} \right]_{t} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{w} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{w} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal}})_{d} \right]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{w} \\ \left[(\operatorname{GlcNAc-\operatorname{Gal})_{d} \right]_{h} - (\operatorname{Gal})_{m} - (\operatorname{Gal})_{m} - (\operatorname{Cal})_{m} - (\operatorname{Cal})_{$$

a-d, i, q-u, w (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51A

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```
CHO, BHK, 293 cells, Vero expressed Remicade.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

galactosyltransferase, UPD-Gal
 CMP-SA-PEG, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = PEG.
```

FIG. 51B

```
CHO, BHK, 293 cells, Vero or fungal expressed Remicade.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

1. galactosyltransferase, UPD-Gal-PEG

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

FIG. 51C

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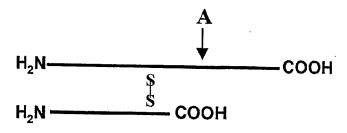
Fungi expressed Remicade. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 51D

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$$\mathbf{A} \leftarrow \begin{array}{c} \text{(Fuc)}_{i} \\ \text{GlcNAc-GlcNAc-Man} \\ \text{([GlcNAc-(Gal)_{a}]_{e}-(Sia)_{j}-(R)_{v})_{r}} \\ \text{(R')}_{n} \\ \text{(R')}_{n} \\ \text{([GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x})_{t}} \\ \text{([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u}} \\ \text{([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y}} \\ \text{([GlcNAc-(G$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 52A

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```
CHO, BHK, 293 cells, Vero expressed Reopro. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 52B

```
Insect cell expressed Reopro.
a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1;
z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 52C

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Yeast expressed Reopro. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose or

1. Endo-H

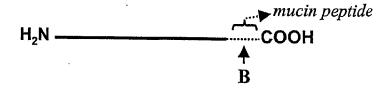
polysaccharide.

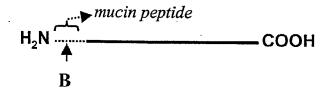
2. Galactosyltransferase, UDP-Gal-PEG

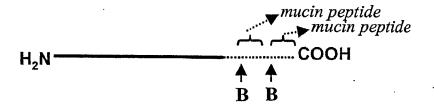
a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 52D

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 52E

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CHO, BHK, 293 cells, Vero expressed
Reopro-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 52F

Insect cell expressed Reopro-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 52G

240/498

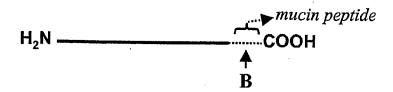
E. coli expressed Reopro-mucin fusion protein. a-e=0.

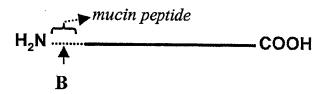
- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 52H

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$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{e}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 521

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E. coli expressed Reopro-mucin fusion protein. a-e, n = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 52J

E. coli expressed Reopro-mucin fusion protein. a-e, n = 0.

- GalNAc Transferase,
 UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 52K

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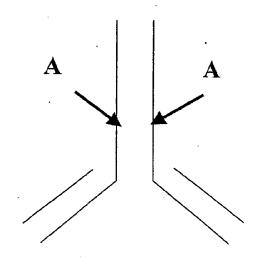
E. coli expressed Reopro(N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 52L

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc} - (\operatorname{Gal})_{a} \end{bmatrix}_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \end{bmatrix}_{r} \\ \left[(\operatorname{GlcNAc} - (\operatorname{Gal})_{b})_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \end{bmatrix}_{s} \\ \left[(\operatorname{GlcNAc} - (\operatorname{Gal})_{b})_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \end{bmatrix}_{t} \\ \left[(\operatorname{GlcNAc} - (\operatorname{Gal})_{d})_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{u} \right]_{q}$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotopecomplex, drug, glycoconjugate.
R' = H, sugar, glycoconjugate.

FIG. 53A

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```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.
```

FIG. 53B

```
CHO, BHK, 293 cells, Vero or fungal expressed Rituxan.

a, c, e, g, i, r, t (independently selected) = 0 or 1;

b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

1. galactosyltransferase, UPD-Gal-drug

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

FIG. 53C

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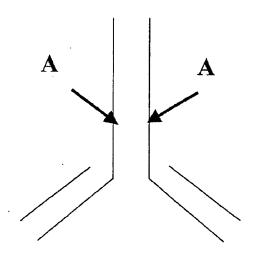
Fungi expressed Rituxan. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 53D

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$$A \leftarrow GlcNAc-Man \qquad Man \begin{bmatrix} [GlcNAc-(Gal)_a]_e - (Sia)_j - (R)_v \end{bmatrix}_r \\ [GlcNAc-(Gal)_b]_f - (Sia)_k - (R)_w \end{bmatrix}_s \\ Man \begin{bmatrix} [GlcNAc-(Gal)_b]_f - (Sia)_l - (R)_w \end{bmatrix}_t \\ [GlcNAc-(Gal)_c]_g - (Sia)_l - (R)_x \end{bmatrix}_t \\ [GlcNAc-(Gal)_d]_h - (Sia)_m - (R)_y \end{bmatrix}_u \\ = Q_t - Q_t$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, glycoconjugate, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 53E

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```
CHO, BHK, 293 cells, Vero or transgenic animal
expressed Rituxan,
a, c, i (independently selected) = 0 or 1;
```

```
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
```

q, z = 1.

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
  when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 53F

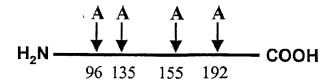
```
Fungi, yeast or CHO expressed Rituxan.
e, g, i, r, t, v, x (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1;
R (independently selected) = mannose, oligomannose,
polymannose.
```

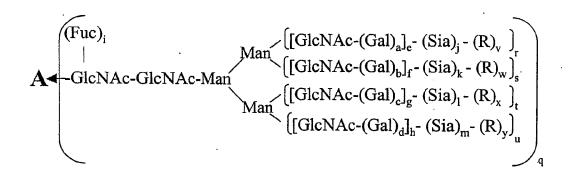
- 1. mannosidases (alpha and beta)
- 2. GNT-I,II, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal-radioisotope

```
a-m, r-z=0; q, n=1;
R' = -Gal-radioisotope complex.
```

FIG. 53G

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a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = mannose, polymer.

FIG. 54A

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```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 54B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 54C

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```
NSO expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 54D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 54E

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CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt

2. H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 54F

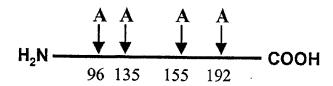
CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

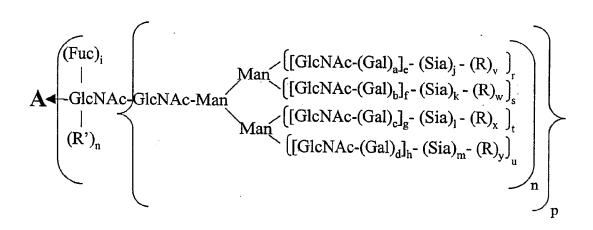
1. CMP-SA, poly- α 2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 54G

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a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100. R = polymer, linker, mannose. R' = H, sugar, glycoconjugate.

FIG. 54H

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```
Insect, yeast or fungi cell expressed AT III. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1; p = 1.
```

1. GNT 1, UDP-GlcNAc-PEG

```
a, i, q, r, -u (independently selected) = 0 or 1;
b-g, j-n, s-u, w-y = 0; p = 1;
v (independently selected) = 1,
when a (independently selected) is 1;
R = PEG.
```

FIG. 541

```
Yeast expressed AT III.

a-n = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 54J

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CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

```
a-m, q-u (independently selected) = 0 or 1;

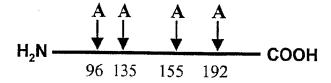
p = 1; n = 0;

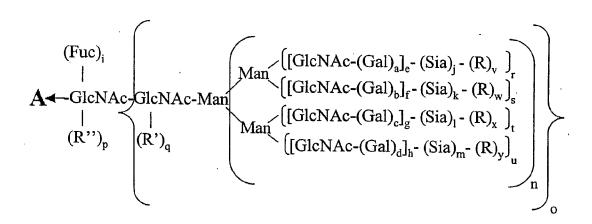
v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 54K

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a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer.

R', R" (independently selected) = sugar, glycoconjugate.

FIG. 54L

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```
Yeast expressed AT III.

a-h, i-m, p, q = 0;

R (independently selected) = mannose,
oligomannose, polymannose;
r-u, v-y (independently selected) = 0 or 1;
n, o = 1.
```

- 1. endoglycanase
- ▼ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

FIG. 54M

```
Plant expressed AT III.

a-d, f-h, j-m, p, s-u, v-y = 0;

e, i, q, r (independently selected) = 0 or 1;

n, o = 1;

R' = xylose.
```

- 1. xylosidase
- 3. Galactosyl transferase, UDP-Gal-PEG

```
b-d, f-h, j-m, p, q, s-u, w-y = 0;
a, e, i, r (independently selected) = 0 or 1;
n, o = 1; R = PEG.
```

FIG. 54N

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CHO, BHK, 293 cells, Vero, transgenic animal expressed AT III.

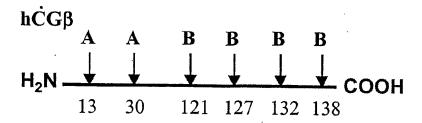
a-h, i-o, r-u (independently selected) = 0 or 1; p, q, v-y=0.

> 1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 540

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hCG
$$\alpha$$

$$H_2N$$

$$52$$

$$78$$
A
A
A
COOH

$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{o} \\ & | \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{bmatrix}_{q}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer

FIG. 55A

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CHO, BHK, 293 cells, insect cell, Vero expressed hCG a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0

1. Sialidase

2. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h = 1 to 3; i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; j-m, v-y (independently selected) = 0 or 1; R = PEG; z = 0.

FIG. 55B

Insect cell, yeast, fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- ♦ 2. CMP-SA-PEG, ST3Gal3

b, d, f, h, k, m, o, p, s, u, w, y, z = 0;
a, c, e, g, i, n, q, r, t (independently selected) = 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
R = PEG.

FIG. 55C

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```
CHO, BHK, 293 cells, insect cell,
Vero expressed hCG
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.
```

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 3. CMP-SA-PEG, ST3Gal1

```
a-h, i-o, q, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 55D

```
CHO, BHK, 293 cells, insect cell or

Vero expressed hCG

a-g, n, q = 1; h = 1 to 3;

j-m, i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m, v-y (independently selected) = 0 or 1;

R = PEG; z = 0.
```

FIG. 55E

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Insect cell, yeast or fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 and 2, UDP-GlcNAc-PEG

e, g, i, n, q, r, t, v, x (independently selected) = 0 or 1; a-d, f, h, j-m, o, p, s, w, y, z = 0; R = PEG.

FIG. 55F

Insect cell, yeast or fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc-PEG

e, i, n, q, r, v (independently selected) = 0 or 1; a-d, g, f, h, j-m, o, p, s, t, w-z = 0; R = PEG.

FIG. 55G

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```
CHO, BHK, 293 cells, insect cell or

Vero expressed hCG

a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1; v-z = 0

1. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h = 1 to 3;
i, o (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, p, z (independently selected) = 0 or 1;
R = PEG; v-y = 0.
```

FIG. 55H

```
a-g, n, q = 1; h = 1 to 3;

j-m, i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1; v-z = 0

1. CMP-SA-PEG, α2,8-ST

a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m (independently selected) = 0 to 2;
```

v-y (independently selected) = 1, when j-m (independently selected) is 2; R = PEG; z = 0.

CHO, BHK, 293 cells, Vero expressed hCG

FIG. 551

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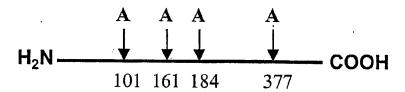
```
CHO, BHK, 293 cells, Vero expressed hCG a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0
```

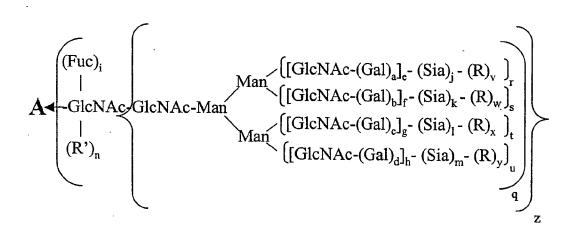
1. CMP-SA, poly- α 2,8-ST

a-i, j-q, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-100; R = Sia.

FIG. 55J

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a-d, i, n, q-u, z (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100; R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 56A

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CHO, BHK, 293 cells, insect cells, Vero expressed and secreted alpha-galactosidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

1. Endo-H

2. Galactosyltransferase, UDP-Gal-PEG-transferrin

```
a-h, i-m, q-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1; and when z = 0 and q = 1,

then n (independently selected) = 0 or 1;

R' = Gal-PEG-transferrin.
```

FIG. 56B

CHO, BHK, 293 cells, Insect cells,

Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y
= 0; and when a-n = 0, then r-u (independently selected) = 0
or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

Sialidase
 CMP-SA-linker-Mannose-6-phosphate

ST3Gal3

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = mannose-6-phosphate; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

FIG. 56C

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NSO expressed alpha-galactosidase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = mannose-6 phosphate

FIG. 56D

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;
n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.

FIG. 56E

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```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

1. mannosyltransferase, GDP-mannose-linker-ApoE

```
a-i = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate;
v-y (independently selected) = 0 or 1;
R = mannose-linker-ApoE.
```

FIG. 56F

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

1. endo-H

2. galactosyltransferase, UDP-Gal-linker-alpha2-macroglobulin

a-m, r-z=0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.

FIG. 56G

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```
Insect cell, yeast, fungi expressed alpha-galactosidase.

a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate

e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

FIG. 56H

```
Insect cell, yeast, fungi expressed
alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc
```

2. galactosyltransferase, UDP-Gal-PEG-transferrin

a, e, i, q, r, v (independently selected) = 0 or 1; b-d, f-h, j-n, s-u, w-y = 0; z = 1; R = PEG-transferrin.

FIG. 561

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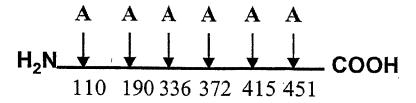
```
Insect cell, yeast, fungi expressed
alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

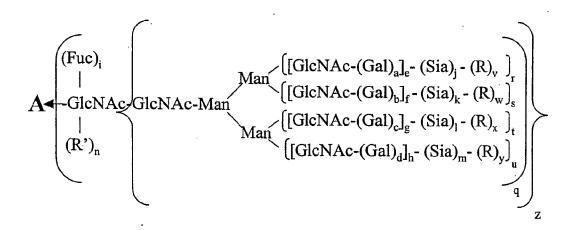
- 1. GNT-1 and 2, UDP-GlcNAc
- 2. galactosyltransferase, UDP-Gal
- 3. sialyltransferase, CMP-SA-PEG-melanotransferrin

a, c, e, g, i, j, l, q, r, t, v, x (independently selected) = 0 or 1; b, d, f, h, k, m, n, s, u, w, y = 0; z = 1; R = PEG-melanotransferrin.

FIG. 56J

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a-d, i, n, q-u, z (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100; R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 57A

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CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- 1. Endo-H
 - 2. Galactosyltransferase, UDP-Gal-PEG-transferrin

```
a-h, i-m, q-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1; and when z = 0 and q = 1, then n
(independently selected) = 0 or 1; R' = Gal-PEG-transferrin.
```

FIG. 57B

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- 1. Sialidase
- 2. CMP-SA-linker-Mannose-6-phosphate ST3Gal3

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = mannose-6-phosphate; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

FIG. 57C

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```
NSO expressed alpha-iduronidase.
a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1;
v-y = 0; Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate
```

FIG. 57D

```
CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

FIG. 57E

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CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.

mannosyltransferase,
 GDP-mannose-linker-ApoE

```
a-i = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1; j-m (independently
selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate;
v-y (independently selected) = 0 or 1;
R = mannose-linker-ApoE.
```

FIG. 57F

CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.

a-i, v-y = 0; q (independently selected) = 0 or 1;

z = 1; r-u (independently selected) = 0 or 1;

j-m (independently selected) = 0-100;

Sia = mannose or mannose with mannose-6-phosphate.

1. endo-H

2. galactosyltransferase, UDP-Gal-linker-alpha2-macroglobulin

a-m, r-z = 0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.

FIG. 57G

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```
Insect cell, yeast, fungi expressed alpha-iduronidase.

a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate

e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

FIG. 57H

```
Insect cell, yeast, fungi expressed
alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc
2. galactosyltransferase,
UDP-Gal-PEG-transferrin

a, e, i, q, r, v (independently selected) = 0 or 1;
b-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-transferrin.
```

FIG. 571

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```
Insect cell, yeast, fungi expressed
alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT-1 and 2, UDP-GlcNAc
- 2. galactosyltransferase, UDP-Gal
- 3. sialyltransferase, CMP-SA-PEG-melanotransferrin

```
a, c, e, g, i, j, l, q, r, t, v, x

(independently selected) = 0 or 1;
b, d, f, h, k, m, n, s, u, w, y = 0; z = 1;
R = PEG-melanotransferrin.
```

FIG. 57J

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FIG. 58A

FIG. 58B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

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FIG. 59A

GCGCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA ATTTTTAATTGTTTTATCATTCTTTGCAATAAAAACATTAACTTTAT ACTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA TAGATACACAGTGTATATGTGATTAAAAATATAATGGGAGATTCAATC AATAATGAAAAAATGTGGTGAGAAAACAGCTGAAAACCCATGTA AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA CCTTTGCTTTACTGGTGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT GCTCTGTGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA GACTCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT TCCAAAGAATCACTCTCTATCTGAAAGAAGAAATACAGCCCTTGT GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCA ACAAACTTGCAAGAAAGTTAAGAAGTAAGGAATGAAAACTGGTTCA ACATGGAAATGATTTCATTGATTCGTATGCCAGCTCACCTTTTTATG ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG ATCTATTTAAAATATTTTAAAAATATTATTTAACTATTTATAAAAAC AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA CATTGAACTTTTGCTATGGAACTTTTGTACTTGTTTATTCTTTAAAATG AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA CTTCATTTGTCCATCAATATTATATTCAAGATATAAGTAAAAATAAAC TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTGTATGAAAA AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT ATGAAGAGAAGAAGGAACG

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FIG. 59B

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu

FIG. 59C

FIG. 59D

Met Ala Leu Leu Phe Pro Leu Leu Ala Ala Leu Val Met Thr Ser Tyr Ser Pro Val Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr Leu Val Leu Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser Gln Leu Gln Lys Ala His Val Met Ser Val Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu His Gln Gln Leu Gln His Leu Glu Thr Cys Leu Leu Gln Val Val Gly Glu Gly Glu Ser Ala Gly Ala Ile Ser Ser Pro Ala Leu Thr Leu Arg Arg Tyr Phe Gln Gly Ile Arg Val Tyr Leu Lys Glu Lys Lys Tyr Ser Asp Cys Ala Trp Glu Val Val Arg Met Glu Ile Met Lys Ser Leu Phe Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp Leu Gly Ser Ser

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FIG. 60A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAAGA AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAAC TGGAGAAAGAATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT ${\tt CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC}$ AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT GAAAGGACACTAGAAGATTTTGAAATTTTATTAAATTATGAGTTATT TTTATTTAT TTAAATTTTTTGGAAAATAAATTATTTTTGGTGC

FIG. 60B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Cys Phe Ser Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly ArgLeu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

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FIG. 61A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG GGCTGCCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT CCTGCACCGGCGCGCGCCCAACGCGTTCCTGGAGGAGCTGCGGC CGGGCTCCCTGGAGAGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA GAATGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC CAGCTGATCTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG TGACCACACGGGCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT CTCTGCTGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA AGGCCGAATTGTGGGGGGCAAGGTGTCCCAAAGGGGAGTGTCCA TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC CTCAGCGAGCACGGGGATGAGCAGAGCCGGCGGGTGGCGCAGG GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG CCCCTCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG CGCCACGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA CTCCTGCAAGGGGACAGTGGAGGCCCACATGCCACCCACTACCGGG GCACGTGGTACCTGACGGCATCGTCAGCTGGGGCCAGGGCTGCGCA ACCGTGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC TGCGAGCCCCATTTCCC

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FIG. 61B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Gly Leu Gln Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Glu Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

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FIG. 62A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA GTATGGAAGAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT GTTCTGTGCTGCCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA TGGAATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT GGAATTGAAAATTAACAG

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FIG. 62B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe LeuAsp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asp Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

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FIG. 63A

FIG. 63B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

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FIG. 63C

FIG. 63D

Met Lys Thr Leu Gln Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

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FIG. 64A

CCCGGAGCCGGGCCACCGCGCCCGCTCTGCTCCGACACCGC GCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT GCACCGCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG CGCGCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGGG GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG CTCCCTCTGGGCCTCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG AGAATATCACGACGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT GGAGGTCGGGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG AAGCCATCTCCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC GTCGAGGGCTCTCAGCTCAGCCCAGCCTGTCCCATGGACACTCCA GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG GTCTCACGGCATGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA ACTGAAACCACCAAAAAAAAAAAAA

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FIG. 64B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

FIG. 65

Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp

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FIG. 66A

ATGTGGCTGCAGAGCCTGCTGCTCTTTGGGCACTGTGGCCTGCAGCAT CTCTGCACCCGCCCGCTCGCCCAGCCCCAGCACGCAGCCCTGGGAGC ATGTGAATGCCATCCAGGAGGCCCGGCGTCTCCTGAACCTGAGTAGA GACACTGCTGAGATGAATGAAACAGTAGAAGTCATCTCAGAAAT GTTTGACCTCCAGGAGCCGACCTGCCTACAGACCCGCCTGGAGCTGT ACAAGCAGGGCCTGCGGGGCAGCCTCACCAAGCTCAAGGGCCCCTTG ACCATGATGGCCAGCCACTACAAGCAGCACTGCCCTCCAACCCCGGA AACTTCCTGTGCAACCCAGATTATCACCTTTGAAAGTTTCAAAGAGA ACCTGAAGGACTTCTGCTTGTCATCCCCTTTGACTGCTGGGAGCCAG TCCAGGAGTGA

FIG. 66B

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

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FIG. 67A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAAATTGTCTCCTTTTACTTCAAACT
TTTTAAAAAACTTTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAGCTGACTAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACTCATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAAAACAGGGAAGCGAAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCGAAGAGCATCCCAGTAA

FIG. 67B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

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FIG. 68A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT CCTGCTGGCAGGCCTGTGCTGCCTGGCTGAGGA TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCACCAA TATCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTGA ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC ACTGTCAACTTCGGGGACACCGAAGAGGGCCAAGAAACAGATCAACG ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG AAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAG CTGGGTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG CTGACCTCTCCGGGGTCACAGAGGGAGGCACCCCTGAAGCTCTCCAAG GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCGA GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC AACTGCCTCTCGCTCCTCAACCCCTCCCTCCATCCCTGGCCCCCTCC CTGGATGACATTAAAGAAGGGTTGAGCTGG

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FIG. 68B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr Gln Lys

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. FIG. 69A-1

GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT GCCCGCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCGACCTTTCCT GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG GGATTTGGAGGGCCATGACAGATGCTGCTGCTCTCAACATCCTTGCC CTGTCACCCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC TTGCCAGCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG GTGAATGGGAAGGGTCACTCAAGGGACAGCCCGGAGACATCTACC ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC TTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG TGACTAAAGAGGCCACGCCAGTGTGAGCTTACAGCGACGT

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FIG. 69A-2

FIG. 69B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Gln Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

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FIG. 70A

AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG GGGCACCTGCCAGCAGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC AGCGGAGAGTGCCCGAGTGCACCAACTGGAACAGCAGCGCGTTG GCCCAGAAGCCCTACAGCGGGGGGGGGGGCCAGACGCCATCAGGCTGG GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT GCAGCACCCCTGCCTGCTGAGGGAAACAGTGACTGCTACTTTGGG AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC CTCCTGCCTCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG GAGGGCTCTTCGCCGACATCGCCTCCCACCCTGGCAGGCTGCCATCT TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT TGCGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG ${\tt CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC}$ CTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACT GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGCCC CAGGCAAACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGCCATCATCAGCT GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

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FIG. 70B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Glu Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro

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FIG. 71A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA TGTACAGGATGCAACTCCTGTCTTGCACTTGCACTAATTCTTGCACTTG TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAA ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA GCTCAAAGCAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA AATATTTAAATTTTATTTTTTTGTTGAATGTATGGTTGCTACCTATTG TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT CAAAAATATTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG AAACAAAAAAAAAA

FIG. 71B

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gln Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr

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FIG. 72A-1

ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTTGCGATTCT GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT GTACAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT TCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTGGAAAGCT TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC CTACTCATATCTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTTGCTGTATTTG ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCCTTGATGCA GGATAGGGATGCTGCATCTGCTCGGGCCTAAAATGCACACAG TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTTGTCATATCTCTT CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG ACTATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC TGGGACTATGCTCCCTTAGTCCTCGCCCCGATGACAGAAGTTATAAA AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG TCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAAT TCTGCCAGGAGAATATTCAAATATAAATGGACAGTGACTGTAGAAG ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTTGTCAGTTTG TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA CTGACTTCCTTCTCTCTCTGGATATACCTTCAAACACAAAAT

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FIG. 72A-2

GGTCTATGAAGACACCCCTATTCCCATTCTCAGGAGAAACTGT CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA CACTTCAGGCCACAGCTCCATCACAGTGGGACATGGTATTTACCCC TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG CAGCAACAGATTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT AGCATCTCTTTGTTAAAGACAAACAAAACTTCCAATAATTCAGCAACT AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA AAACATGGAAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG GTAGTAGGAAAGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA TGGTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT TACATGAAAATAATACACACAATCAAGAAAAAAAAATTCAGGAAGA AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC AGATACATGACTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG AACAAAGAAACACACACCTCATTTCTCAAAAAAAGGGGAGGAAGAA AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

FIG. 72A-3

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GAAGAAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA TCTCCATTACCCATTGCAAAGGTATCATCATTTTCCATCTATTAGACCTA TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT TTCTTACAAGGAGCCAAAAAAAAAAACCTTTCTTTAGCCATTCTAACC TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT TCCCTTCTGAGAGTAGCAACAGAAGACTCTCCAA GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAAACAGCT TTTAAGAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT TGAAATGAAGAAGAATTTTGACATTTATGATGAGGATGAAAATC AGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTG CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC GTCCCTATTCCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG GCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAACCA AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT TGCTCTGTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT ATTCATTTCAGTGGACATGTTCACTGTACGAAAAAAAAGAGGGGTA TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTTGAGACAGTGGA

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FIG. 72A-4

AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG CCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC TCTCTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC CACTGCAGCACCTGCCGTCACCTCTCCTCAGCTCCAGG GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT TCTTTGGTGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA CCTATTTCTGCAGCTGCTCCCAGATTACTCCTTCCTTCCAATATAACT AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT ATGTGATGAAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT TAAGCCTCATACGTTTAAAAATAAAACTCTCAGTTGTTTATTATCCTGA TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC TAAGTCCCCTGAAATTATAAAGGCATTCTGTATAAATGCAAATGTGC ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT GACCAATAAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG AAATGATGA

FIG. 72B-1

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asp Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe FIG. 72B-2

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Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro

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Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu As Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile

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FIG. 72B-4

Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr

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FIG. 73A

TCCACCTGTCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA ACATGTGTGTCCAACAGTACTTCTCCAACATTCACTGGTGCAACTGC CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG ACACCATGGGCCGGCCCTGCCTGGAACTCTGCCACTGTCCTTC AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCCTCCAGAAGAAT TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC ATCTACAGGAGGCACCGGGGGGGGCTCTGTCACCTACGTGTGTGGAGG CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC CTCATCCTACACAGGACTACAGCGCTGACACGCTTGCTCACCACAAC GACATTGCCTTGCTGAAGATCCGTTCCAAGGAGGGCAGGTGTGCGCA GCCATCCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG AAGTCACCACAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC CCTGGATCCGCAGTCACACCAAGGAAGAGAATGGCCTGGCCCTCTGA GGGTCCCCAGGGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA AGAT

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FIG. 73B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

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FIG.74A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA TAGACTACTTTTTTTTTTTAAGCAGCAAAAGGAGAAAATTGTCATCA AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC ACCATCATCTCAGGATGAGGGCCATGAAGCTGCTGGGGGGCGCTGCTG GCACTGCCGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG GTCAGGTTCTCCCGGTTCACAGAGGTCAGGGAGTTTGCCATTGTT CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGGCTTGGAGGACG TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT CCCAGTGGTCATCCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT ATGACAGGATCGTGGTTGCAGGGATGCTCCGAGGCGCCGTTGTTC CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG CTGAAGTGAGCACCCCTCCCCACACCAGTTGAACTGCAG

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FIG. 74B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Ala Gly Met Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val Glu Val Met Leu Lys

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FIG. 75A

FIG. 75B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

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FIG. 76A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC GGGCCAGGGTTCACCCCACCACGGCGGTCTTTTGGGGTGGAGCCC TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA GGCGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTCTCTGCGGCGTTTT ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTTGGGTATAC ATTTGA

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FIG. 76B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile

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FIG. 77A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC CTTTTGACAACGCTATGCTCCGCGCCCATCGTCTGCACCAGCTGGCCT TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG GAAGGACATGGCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG CTCTGTGGAGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG TGACCCCTCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT GCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATC

FIG. 77B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

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FIG. 78A

TTATCTTTTGTCCTTGCTGCTCATTGGCTTCTGGGACTGCGTGACCTGT CACGGGAGCCTGTGGACATCTGCACAGCCAAGCCGCGGGACATTCC CATGAATCCCATGTGCATTTACCGCTCCCGGAGAAGAAGAAGCAACTG AGGATGAGGCTCAGAACAGAAGATCCCGGAGGCCACCAACCGGCG TGTCTGGGAACTGTCCAAGGCCAATTCCCGCTTTGCTACCACTTTCTA TCAGCACCTGGCAGATTCCAAGAATGACAATGATAACATTTTCCTGTC ACCCCTGAGTATCTCCACGGCTTTTGCTATGACCAAGCTGGGTGCCTG TAATGACACCTCCAGCAACTGATGGAGGTATTTAAGTTTGACACCAT ATCTGAGAAAACATCTGATCAGATCCACTTCTTTTTTTTCCAAACTGAA CTGCCGACTCTATCGAAAAGCCAACAAATCCTCCAAGTTAGTATCAGC CAATCGCCTTTTTGGAGACAAATCCCTTACCTTCAATGAGACCTACCA GGACATCAGTGAGTTATATGGAGCCAAGCTCCAGCCCCTGGACT TCAAGGAAAATGCAGAGCAATCCAGAGCGGCCATCAACAAATGGGTG TCCAATAAGACCGAAGCCGAATCACCGATGTCATTCCCTCGGAAGC CATCAATGAGCTCACTGTTCTGGTGCTGGTTAACACCATTTACTTCAA TGTTCTACAAGGCTGATGGAGAGTCGTGTTCAGCATCTATGATGTACC AGGAAGGCAAGTTCCGTTATCGGCGCGTGGCTGAAGGCACCCAGGTG CTTGAGTTGCCCTTCAAAGGTGATGACATCACCATGGTCCTCATCTTG CCCAAGCCTGAGAAGAGCCTGGCCAAGGTGGAGAAGGAACTCACCCC AGAGGTGCTGCAGGAGTGGCTGGATGAATTGGAGGAGATGATGCTGG TGGTCCACATGCCCCGCTTCCGCATTGAGGACGGCTTCAGTTTGAAGG AGCAGCTGCAAGACATGGGCCTTGTCGATCTGTTCAGCCCTGAAAAG TCCAAACTCCCAGGTATTGTTGCAGAAGGCCGAGATGACCTCTATGTC TCAGATGCATTCCATAAGGCATTTCTTGAGGTAAATGAAGAAGGCAG TGAAGCAGCTGCAAGTACCGCTGTTGTGATTGCTGGCCGTTCGCTAAA ${\tt CCCCAACAGGGTGACTTTCAAGGCCAACAGGCCTTTCCTGGTTTTTAT}$ AAGAGAAGTTCCTCTGAACACTATTATCTTCATGGGCAGAGTAGCCA ACCCTTGTGTTAAGTAA

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FIG. 78B

Met Tyr Ser Asn Val Ile Gly Thr Val Thr Ser Gly Lys Arg Lys Val Tyr Leu Leu Ser Leu Leu Ile Gly Phe Trp Asp Cys Val Thr Cys His Gly Ser Pro Val Asp Ile Cys Thr Ala Lys Pro Arg Asp Ile Pro Met Asn Pro Met Cys Ile Tyr Arg Ser Pro Glu Lys Lys Ala Thr Glu Asp Glu Gly Ser Glu Gln Lys Ile Pro Glu Ala Thr Asn Arg Arg Val Trp Glu Leu Ser Lys Ala Asn Ser Arg Phe Ala Thr Thr Phe Tyr Gln His Leu Ala Asp Ser Lys Asn Asp Asn Asp Asn Ile Phe Leu Ser Pro Leu Ser Ile Ser Thr Ala Phe Ala Met Thr Lys Leu Gly Ala Cys Asn Asp Thr Leu Gln Gln Leu Met Glu Val Phe Lys Phe Asp Thr Ile Ser Glu Lys Thr Ser Asp Gln Ile His Phe Phe Ala Lys Leu Asn Cys Arg Leu Tyr Arg Lys Ala Asn Lys Ser Ser Lys Leu Val Ser Ala Asn Arg Leu Phe Gly Asp Lys Ser Leu Thr Phe Asn Glu Thr Tyr Gln Asp Ile Ser Glu Leu Val Tyr Gly Ala Lys Leu Gln Pro Leu Asp Phe Lys Glu Asn Ala Glu Gln Ser Arg Ala Ala Ile Asn Lys Trp Val Ser Asn Lys Thr Glu Gly Arg Ile Thr Asp Val Ile Pro Ser Glu Ala Ile Asn Glu Leu Thr Val Leu Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Leu Trp Lys Ser Lys Phe Ser Pro Glu Asn Thr Arg Lys Glu Leu Phe Tyr Lys Ala Asp Gly Glu Ser Cys Ser Ala Ser Met Met Tyr Gln Glu Gly Lys Phe Arg Tyr Arg Arg Val Ala Glu Gly Thr Gln Val Leu Glu Leu Pro Phe Lys Gly Asp Asp Ile Thr Met Val Leu Ile Leu Pro Lys Pro Glu Lys Ser Leu Ala Lys Val Glu Lys Glu Leu Thr Pro Glu Val Leu Gln Glu Trp Leu Asp Glu Leu Glu Glu Met Met Leu Val Val His Met Pro Arg Phe Arg Ile Glu Asp Gly Phe Ser Leu Lys Glu Gln Leu Gln Asp Met Gly Leu Val Asp Leu Phe Ser Pro Glu Lys Ser Lys Leu Pro Gly Ile Val Ala Glu Gly Arg Asp Asp Leu Tyr Val Ser Asp Ala Phe His Lys Ala Phe Leu Glu Val Asn Glu Glu Gly Ser Glu Ala Ala Ser Thr Ala Val Val Ile Ala Gly Arg Ser Leu Asn Pro Asn Arg Val Thr Phe Lys Ala Asn Arg Pro Phe Leu Val Phe Ile Arg Glu Val Pro Leu Asn Thr Ile Ile Phe Met Gly Arg Val Ala Asn Pro Cys Val Lys

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FIG. 79A

ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCG
GTGTTTCTGCATGTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAG
AATGCACGCTACAGGAAAACCCATTCTTCTCCCAGCCGGGTGCCCCA
ATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCACTCCA
CTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGA
GTCCACTTGCTGTAGCTAAATCATATAACAGGGTCACAGTAATGGG
GGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTGTT
ATTATCACAAATCTTAA

FIG. 79B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

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FIG. 79C

FIG. 79D

Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Leu Ser Met Gly Gly Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln

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FIG. 80A

ATGCGTCCCCTGCGCCCCGCGCGCGCTGCTGGCCTCCTGGCCTCG CTCCTGGCCGCCCCCGGTGGCCCCGGCCGAGGCCCCGCACCTGGT GCAGGTGGACGCGCGCGCGCGCTGTGGCCCCTGCGGCGCTTCTGGA GGAGCACAGGCTTCTGCCCCCCCCCCCACACAGCCAGGCTGACCAG TACGTCCTCAGCTGGGACCAGCAGCTCAACCTCGCCTATGTGGGCGCC GTCCCTCACCGCGCATCAAGCAGGTCCGGACCCACTGGCTGCA GCTTGTCACCACCAGGGGGTCCACTGGACGGGGCCTGAGCTACAACT TCACCCACCTGGACGGTACTTGGACCTTCTCAGGGAGAACCAGCTCC TCCCAGGGTTTGAGCTGATGGGCAGCGCCTCGGGCCACTTCACTGACT TTGAGGACAAGCAGCAGGTGTTTGAGTGGAAGGACTTGGTCTCCAGC CTGGCCAGGAGATACATCGGTAGGTACGGACTGGCGCATGTTTCCAA GTGGAACTTCGAGACGTGGAATGAGCCAGACCACCACGACTTTGACA ACGTCTCCATGACCATGCAAGGCTTCCTGAACTACTACGATGCCTGCT GGCGACTCCTTCCACACCCCACCGCGATCCCCGCTGAGCTGGGGCCTC CTGCGCCACTGCCACGACGTACCAACTTCTTCACTGGGGAGGCGGG CGTGCGGCTGGACTACATCTCCCTCCACAGGAAGGGTGCGCGCAGCT CCATCTCCATCCTGGAGCAGGAGAAGGTCGTCGCGCAGCAGATCCGG CAGCTCTTCCCCAAGTTCGCGGACACCCCCATTTACAACGACGAGGCG GACCCGCTGGTGGGCTGGTCCCTGCCACAGCCGTGGAGGGCGGACGT GACCTACGCGCCATGGTGGTGAAGGTCATCGCGCAGCATCAGAACC TGCTACTGGCCAACACCACCTCCGCCTTCCCCTACGCGCTCCTGAGCA ACGACAATGCCTTCCTGAGCTACCACCCGCACCCCTTCGCGCAGCGCA CGCTCACCGCGCGCTTCCAGGTCAACACACCCGCCGCCGCACGTG CAGCTGTTGCGCAAGCCGGTGCTCACGGCCATGGGGCTGCTGGCGCT GCTGGATGAGGAGCAGCTCTGGGCCGAAGTGTCGCAGGCCGGGACCG TCCTGGACAGCAACCACGGTGGGCGTCCTGGCCAGCGCCCACCGC CCCCAGGCCCGACGCCTGGCGCGCGCGGTGCTGATCTACGC TGCGGCTGCGCGGGTGCCCCCGGCCCGGGCCTGGTCTACGTCACG CGCTACCTGGACAACGGGCTCTGCAGCCCCGACGGCGAGTGGCGGCG CCTGGGCCGGCCGTCTTCCCCACGGCAGAGCAGTTCCGGCGCATGC GCGCGCTGAGGACCCGGTGGCCGCGCGCCCCCTTACCCGCC GGCGGCCTGACCCTGCGCCCCGCGCTGCGGCTGCCGTCTTTTG CTGGTGCACGTGTGCGCCCCGAGAAGCCGCCCGGGCAGGTCAC GCGGCTCCGCCCCTGACCCAAGGGCAGCTGGTTCTGGTCTG GTCGGATGAACACGTGGGCTCCAAGTGCCTGTGGACATACGAGATCC AGTTCTCTCAGGACGGTAAGGCGTACACCCCGGTCAGCAGGAAGCCA TCGACCTTCAACCTCTTTGTGTTCAGCCCAGACACAGGTGCTGTCTCT GGCTCCTACCGAGTTCGAGCCCTGGACTACTGGGCCCGACCAGGCCC CTTCTCGGACCCTGTGCCGTACCTGGAGGTCCCTGTGCCAAGAGGGCC CCCATCCCGGGCAATCCAT GA

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FIG. 80B

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Glu Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro

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FIG. 81A

ATGCAGCTGAGGAACCCAGAACTACATCTGGGCTGCGCGCTTGCGCT TCGCTTCCTGGCCCTCGTTTCCTGGGACATCCCTGGGGCTAGAGCACT GGACAATGGATTGGCAAGGACGCCTACCATGGGCTGCACTGGG AGCGCTTCATGTGCAACCTTGACTGCCAGGAAGAGCCAGATTCCTGC ATCAGTGAGAAGCTCTTCATGGAGATGGCAGAGCTCATGGTCTCAGA AGGCTGGAAGGATGCAGGTTATGAGTACCTCTGCATTGATGACTGTTG GATGGCTCCCCAAAGAGATTCAGAAGGCAGACTTCAGGCAGACCCTC AGCGCTTTCCTCATGGGATTCGCCAGCTAGCTAATTATGTTCACAGCA AAGGACTGAAGCTAGGGATTTATGCAGATGTTGGAAATAAAACCTGC GCAGGCTTCCCTGGGAGTTTTGGATACTACGACATTGATGCCCAGACC TTTGCTGACTGGGGAGTAGATCTGCTAAAATTTGATGGTTGTTACTGT GACAGTTTGGAAAATTTGGCAGATGGTTATAAGCACATGTCCTTGGCC CTGAATAGGACTGGCAGAAGCATTGTGTACTCCTGTGAGTGGCCTCTT TATATGTGGCCCTTTCAAAAGCCCAATTATACAGAAATCCGACAGTAC TGCAATCACTGGCGAAATTTTGCTGACATTGATGATTCCTGGAAAAGT ATAAAGAGTATCTTGGACTGGACATCTTTTAACCAGGAGAGAATTGTT GATGTTGCTGGACCAGGGGGTTGGAATGACCCAGATATGTTAGTGAT TGGCAACTTTGGCCTCAGCTGGAATCAGCAAGTAACTCAGATGGCCCT CTGGGCTATCATGGCTCCTTTATTCATGTCTAATGACCTCCGACA CATCAGCCCTCAAGCCAAAGCTCTCCTTCAGGATAAGGACGTAATTGC CATCAATCAGGACCCCTTGGGCAAGCAAGGGTACCAGCTTAGACAGG GAGACAACTTTGAAGTGTGGGAACGACCTCTCTCAGGCTTAGCCTGG GCTGTAGCTATGATAAACCGGCAGGAGATTGGTGGACCTCGCTCTTAT ACCATCGCAGTTGCTTCCCTGGGTAAAGGAGTGGCCTGTAATCCTGCC TGCTTCATCACACAGCTCCTCCCTGTGAAAAGGAAGCTAGGGTTCTAT GAATGGACTTCAAGGTTAAGAAGTCACATAAATCCCACAGGCACTGT TTTGCTTCAGCTAGAAAATACAATGCAGATGTCATTAAAAGACTTACT TTAA

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FIG. 81B

Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gln Met Ala Leu Trp Ala Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu

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FIG. 82A

ATGGCGCCGTCGCCGTCTGGGCCGCCGTCGGACTGGAGCT CTGGGCTGCGCCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA CGCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCAAG TGCCGCCCGGGCTTCGGCGTGGCCAGACCAGGAACTGAAACATCAGA CGTGGTGTCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCCCCA ACACGATCCCAACACGCAGCCAACTCCAGAACCCAGCACTGCTCC AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG GAGCACTGGCGACTTCCAGTTGGACTGATTGTGGGTGTGAC AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCGGGGAGGCCCGGGC CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT CACAGTGCTCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC AGCCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG GGAGCACCGAAGAGAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTTCCAGGC

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FIG. 82B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser

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FIG. 83A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 83B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 84A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

FIG. 84B

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 85A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGC
ATCCACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCTCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACAAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTGAAGCTTGA
GGAGTCTGGAGGAGCCTTGGTGCAACCTGGAGGATCCATGAAACTCT
CCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGG
TCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACATTATGCGGAGTCTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAGTGCTGTCTACCTGCAA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTC
ACAGTCTCC

FIG. 85B

Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr LeuGln Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser

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FIG. 86A

ATGGAGACACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA GGTTCCACTGGTGACGTCAGGCGAGGCCCCGGAGCCTGCGGGGCAG GGACGCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGC CGAAACCGGCCGGGCCAGCAGCCCTGCGCCCAGGACGCGCTGCAG AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA CCGTCAGTCTTCCCCCCAAAACCCAAGGACACCCTCATGATC TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGC ATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTA CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT CAGCCTGACCTGCTCAAAGGCTTCTATCCCAGCGACATCGCCGT GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG ${\tt CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCTTCTACAGCAAGCTC}$ ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCTCCCGGGAAATGA

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FIG. 86B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Val Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

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FIG. 87

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 88

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Pro Gly Thr Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ala

FIG. 89

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys

FIG. 90

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 91

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

FIG. 92

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr IIe Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Glv

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FIG. 93A

ATGGATTTCAGGTGCAGATTATCAGCTTCCTGCTAATCAGTGCTTCA GTCATAATGTCCAGAGGGCAAATTGTTCTCTCCCAGTCTCCAGCAATC CTGTCTGCATCTCCAGGGGAGAAGGTCACAATGACTTGCAGGGCCAG CTCAAGTGTAAGTTACATCCACTGGTTCCAGCAGAAGCCAGGATCCTC CCCCAAACCCTGGATTTATGCCACATCCAACCTGGCTTCTGGAGTCCC TGTTCGCTTCAGTGGCAGTGGGTCTGGGACTTCTTACTCTCTCACAAT CAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAGCAGT GGACTAGTAACCCACCCACGTTCGGAGGGGGGACCAAGCTGGAAATC

FIG. 93B

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 94A

FIG. 94B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala

333/498 FIG. 95A

GACGTCGCGGCCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGGGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATTGGCTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATAGC GGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACCATGAGGGTCCCCGCTCAGCTCCT GGGGCTCCTGCTCTGGCTCCCAGGTGCACGATGTGATGGTACCAA GGTGGAAATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCT GCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGG ATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAG GACAGCAAGGACACCTACAGCCTCAGCAGCACCCTGACGCTGAG CAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCC ATCAGGGCCTGAGCTCGCCCGTCACAAGAGCTTCAACAGGGGAGAG TGTTGAATTCAGATCCGTTAACGGTTACCAACTACCTAGACTGGATTC GTGACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTG CCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCGTGCCTTCCT TGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGG AAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGGTG GGGTGGGCAGGACAGCAAGGGGGGGGGGAGGATTGGGAAGACAATAGCAG GCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGAC AGCTATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGC ${\tt CCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT}$ GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGT TTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGA

334/498 FIG. 95B

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG TGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

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FIG. 95C

GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA GCTCATTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA GTCTACGAGAAGAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG TTGCCCCTCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTT ATTTGCATAATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCA GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG TAAGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC TGACATAGTTGTGTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT CGTGGCTGGCCACGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG TCACTGAAGCGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG CAGGATCTCCTCACCTTGCTCCTGCCGAGAAAGTATCCATC ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC AGGGGCTCGCCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG CCCGACGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

336/498 FIG. 95D

AATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC CGGCTGGGTGTGGCGACCGCTATCAGGACATAGCGTTGGCTACCCG TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC CGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCG CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT GTGGTTTGTCCAAACTCATCATCTATCTTATCATGTCTGGATCGCGG CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGG AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT TGCGTATTGGGCGCTCTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA GCAAAAGGCCAGCAAAAGGCCGCGTTGC TGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC CAGGCGTTTCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTTGTGCACGAACCCCCGGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA CACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA ACTACGCCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA ${\tt CAAACCACCGCTGGTAGCGGTGGTTTTTTTTTTTTTTTGCAAGCAGCAGATT}$ ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTAC GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA AATGAAGTTTTAAATCAATCTAAAGTATATGAGTAAACTTGGTCTG ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC GAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCA GCCGGAAGGCCCAGAAGTGGTCCTGCAACTTTATCCGCCTC

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FIG. 95E

CAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG
TGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC
GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAAGCGGTT
AGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTG
TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC
CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCAT
TCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAA
TACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATC
ATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCA
GCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGG
CAAAATGCCGCAAAAAAAGGGAATAATTATTGAAGCATTTATCAGGGTTA
TACTCATACTCTTCCTTTTTCAATATTTTGAAGCATTTATCAGGGTTA
TTGTCTCATGAGCGGATACATATTTGAATGTATTTTAGAAAAAATAAACA
AATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCT

338/498 FIG. 96A

GACGTCGCGCCCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGCGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATTGGCTAGGGCGGGACTATGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCGGGAGCCT ATACTTCTGCCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATACC GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT TGTTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT GGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCA CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT CTGGGACTTCTTACTCTCACAATCAGCAGAGTGGAGGCTGAAGATG GAGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC TCTGTTGTGCCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG TGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCA CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTC CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

339/498 FIG. 96B

TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT CCGCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTC TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTGT CGCTGTTGCTACGCGTGTCCCAGGTACAACTGCAGCAGCCTGG GGCTGAGCTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG GCGGTGACTGCTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC AAGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG TCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAG ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA AGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACC ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT GCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT GGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

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FIG. 96C

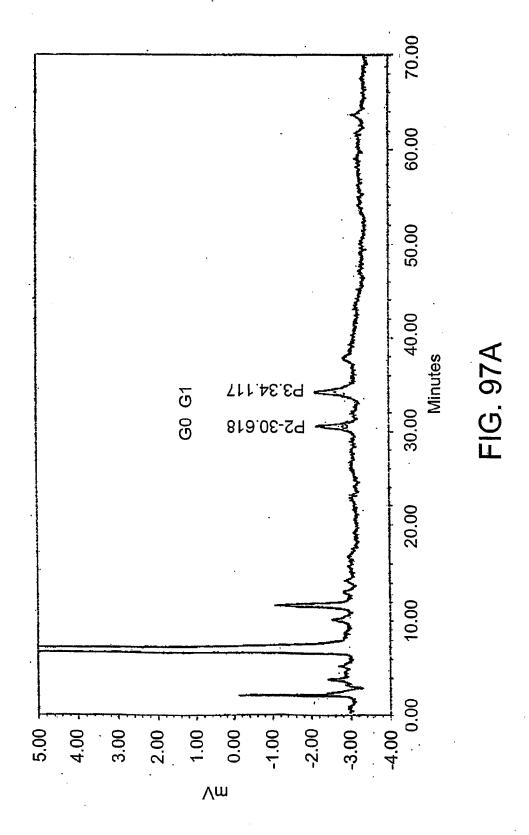
GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG GTGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGC ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG CGCTGGATCTCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT AATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG CGCCAAACTTGACGCCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGC ${\tt CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG}$ CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTGA GGTCCAGGAGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA AGCTATGCATTTTATAAGACCATGGGACTTTTGCTGGCTTTAGATCA GCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCC CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT TCTGGGGGGGGGGGGGGGGGGGGGGGGAGGATTGGGAA GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT CTGCTCACACAGGATAGAGAGGGCAGGGCAGGGCAGAGCATATA AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG

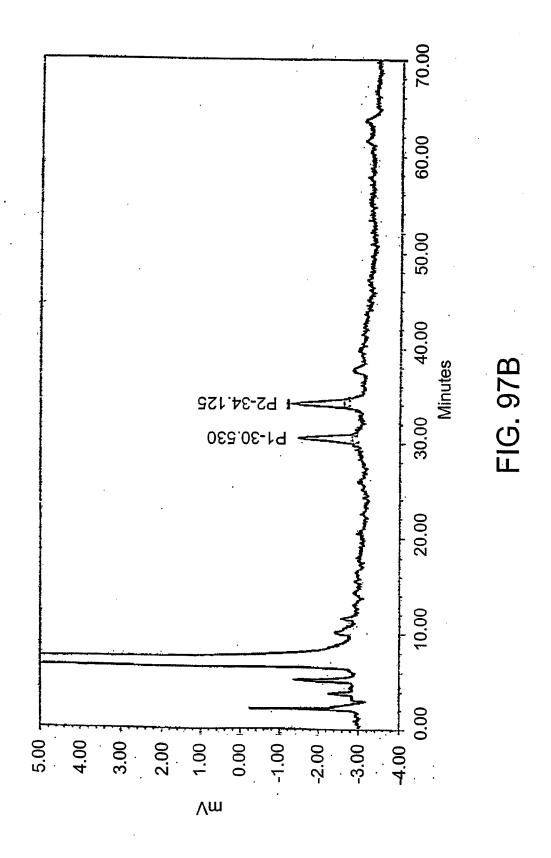
341/498 FIG. 96D

TGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAAGATGGATTGCA CGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTG GGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC AGCGCAGGGCCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGC CCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCCA CGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTG TCATCTCACCTTGCTGCCGAGAAAGTATCCATCATGGCTGATGCA ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCAC CAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGC CAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGCGAG GATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTG GAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTG GCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGA AGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTAT CGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGA GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGA AAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCT CCAGCGCGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTT TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT CACAAATAAAGCATTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAA ACTCATCAATCTATCATGTCTGGATCGCGGCCGCGATCCCGTC GAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTT GCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGC GCTCTTCCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT GCGGCGAGCGGTATCAGCTCACAAAGGCGGTAATACGGTTATCCA CAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCA GCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCC ATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC CCCTGGAAGCTCCCTGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA ATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA GCTGGGCTGTGCACGAACCCCCGTTCAGCCCGACCGCTGCGCCTT ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC

FIG. 96E

GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA AAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGC TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC AAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA ATCAATCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATG CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGCCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC GCACATTTCCCCGAAAAGTGCCACCT





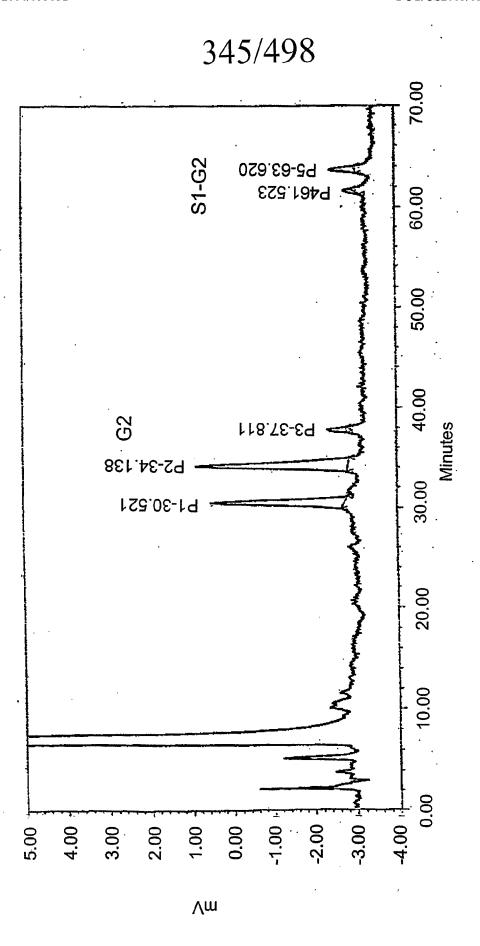


FIG. 97C

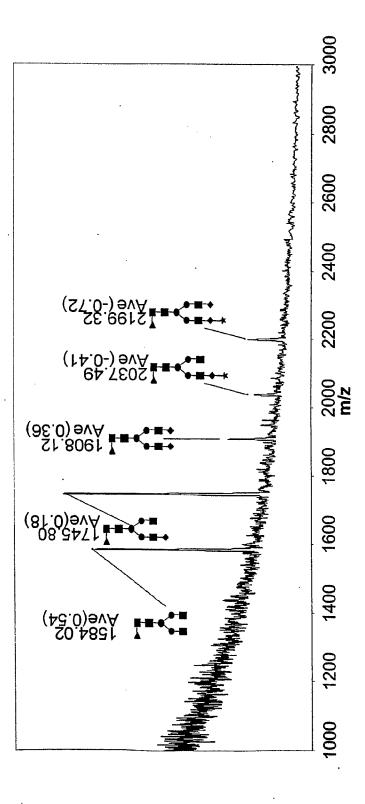
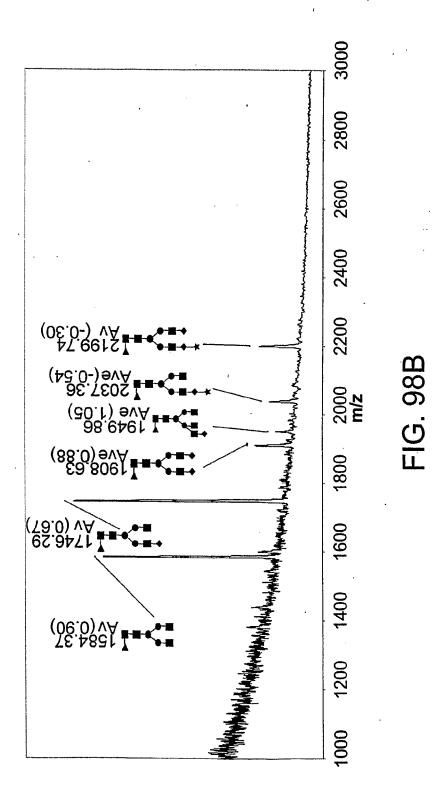


FIG. 98A

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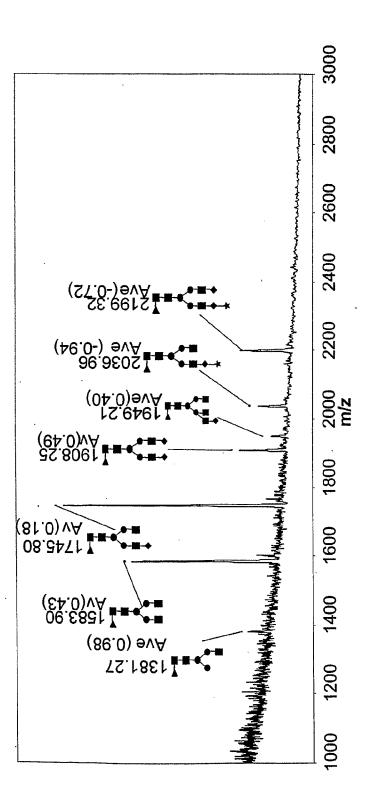
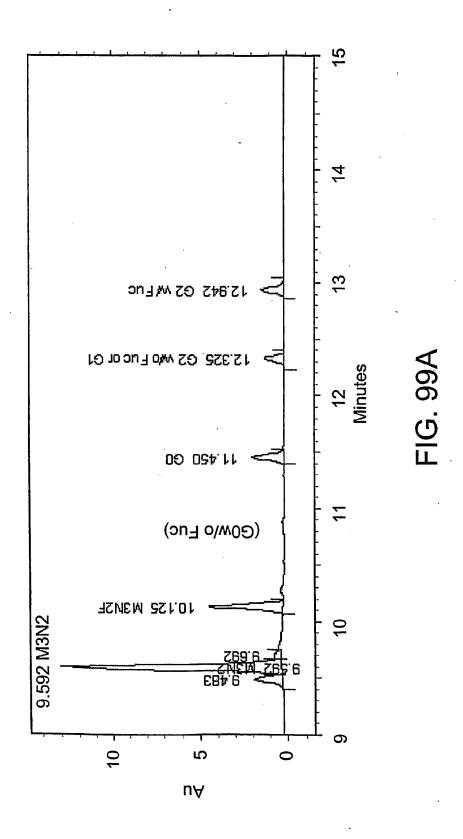
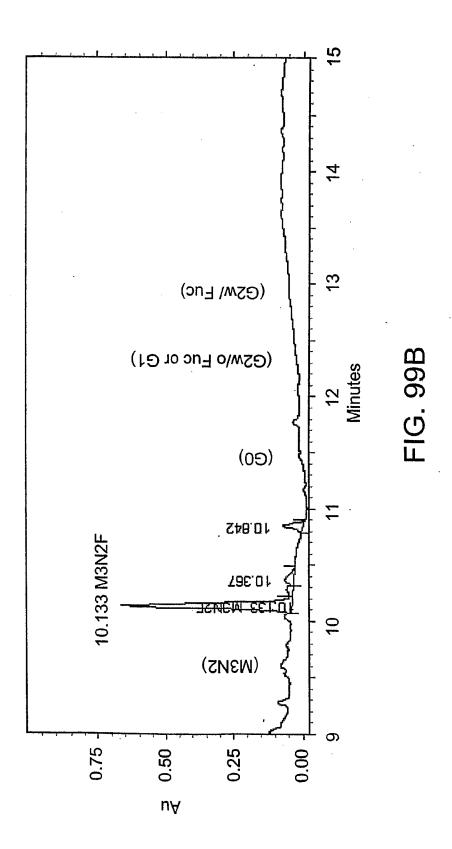
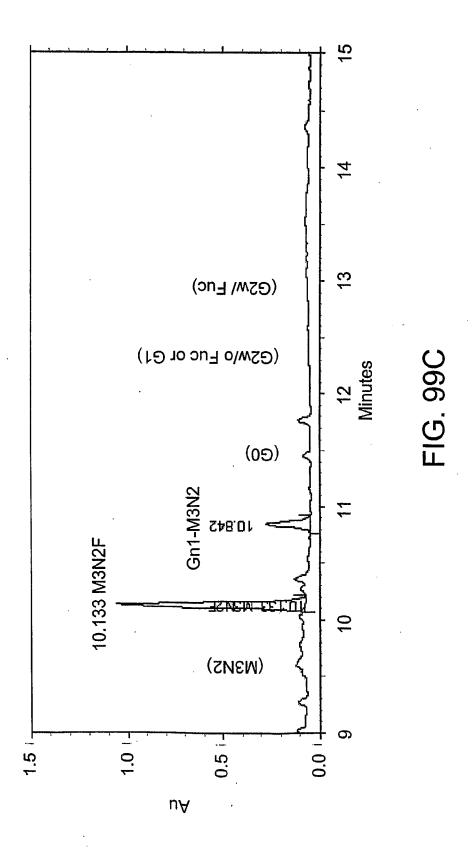


FIG. 98C

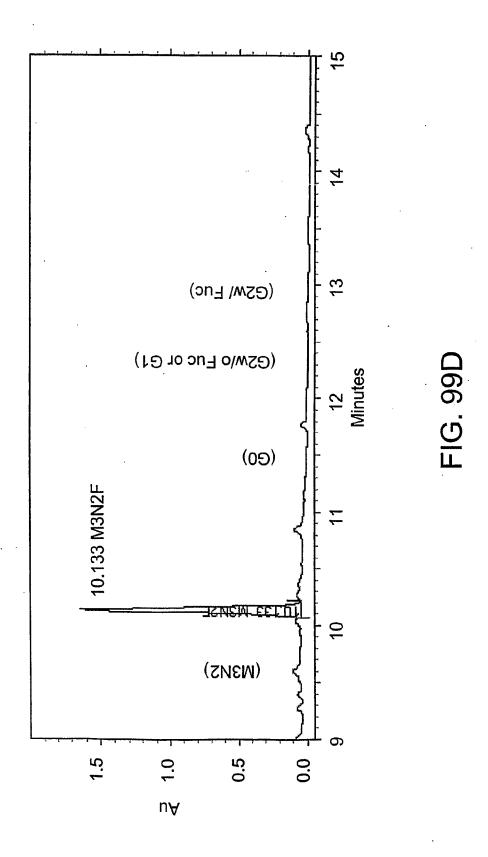




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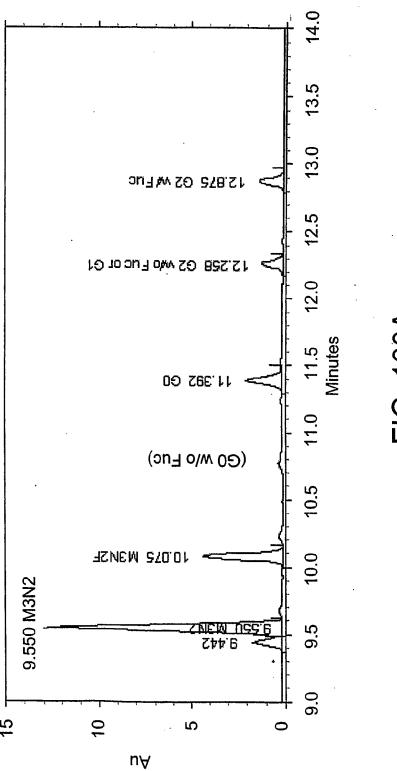
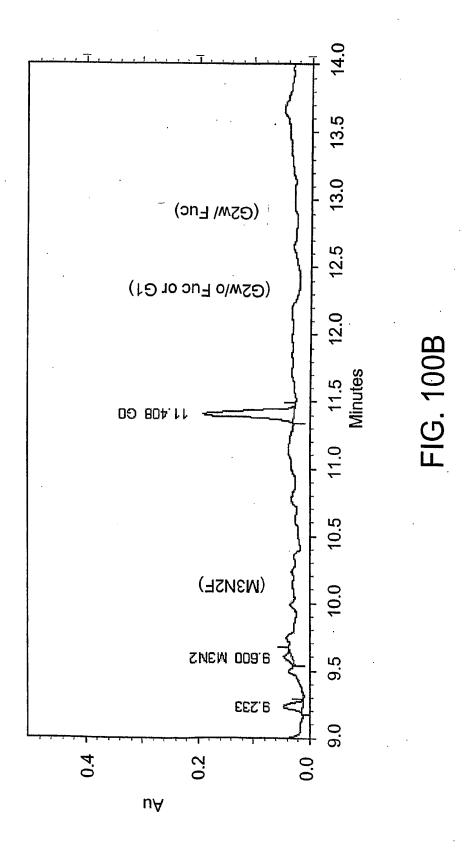
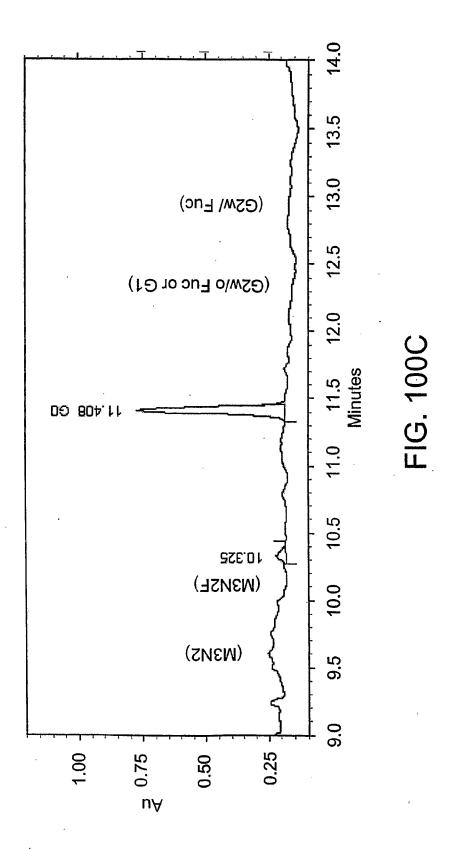
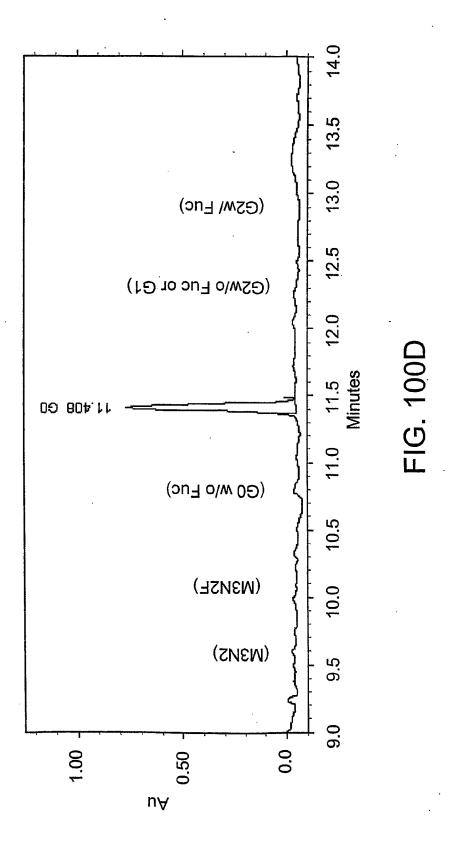
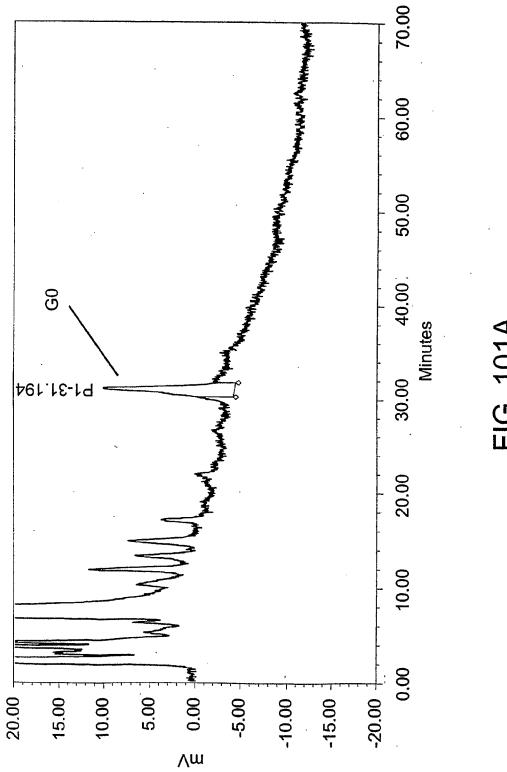


FIG. 100A









-IG. 101A

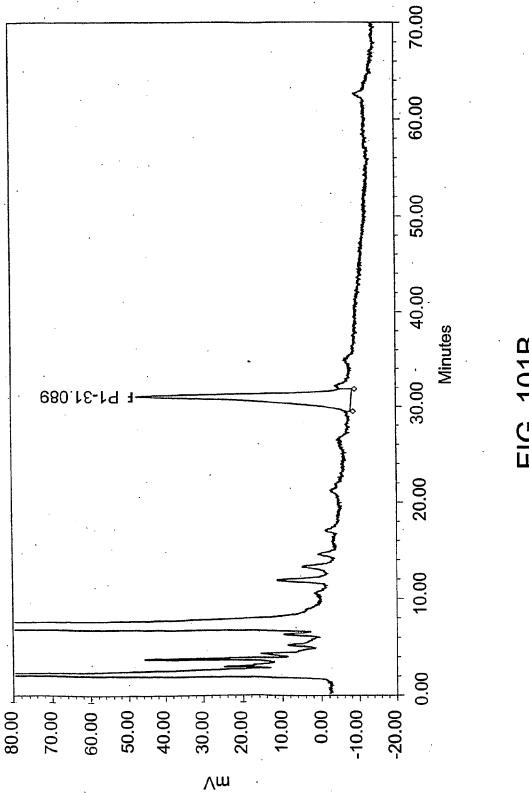
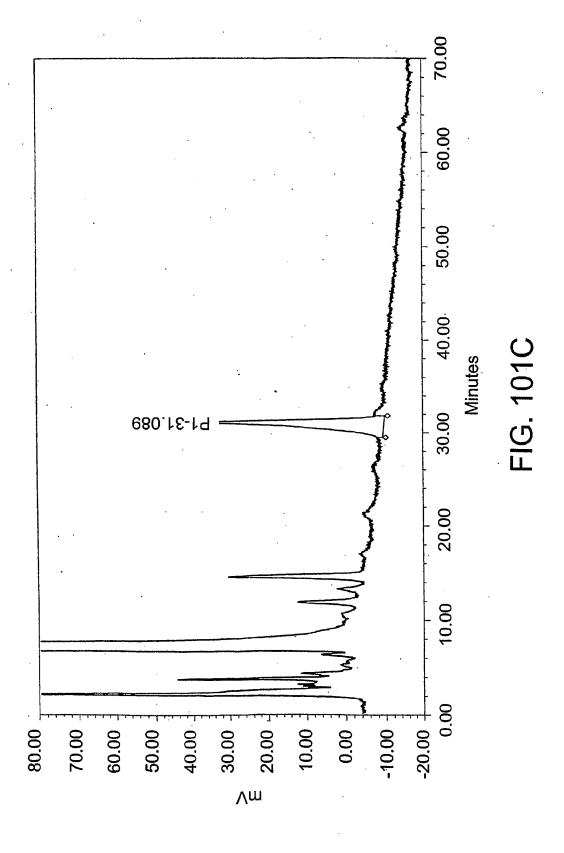


FIG. 101B

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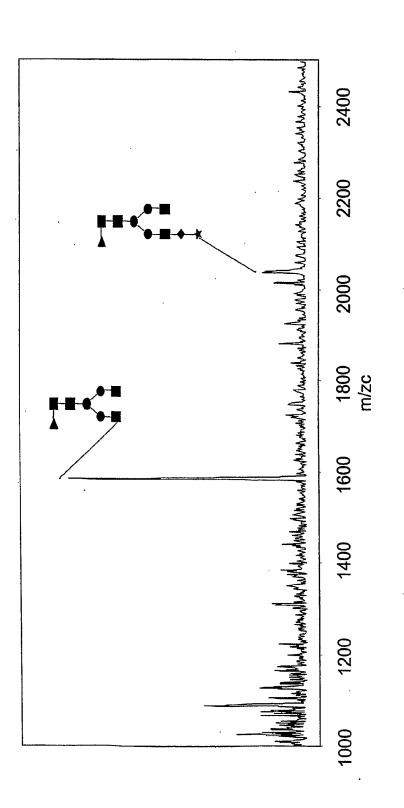


FIG. 102A

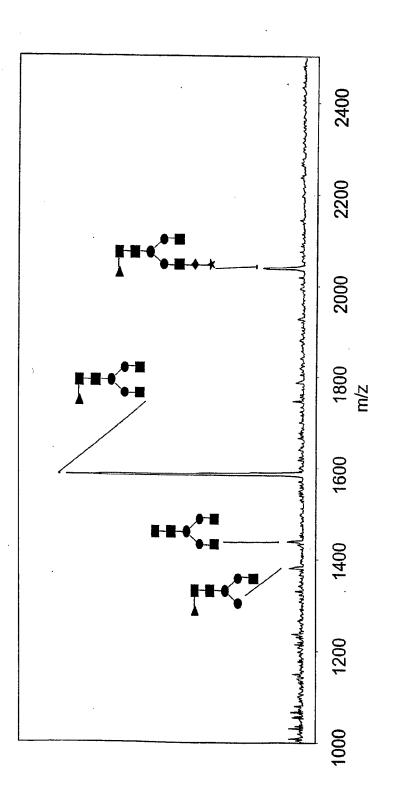


FIG. 102B

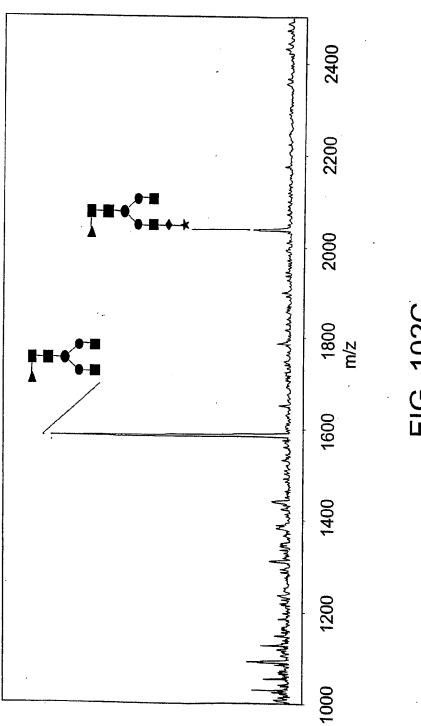
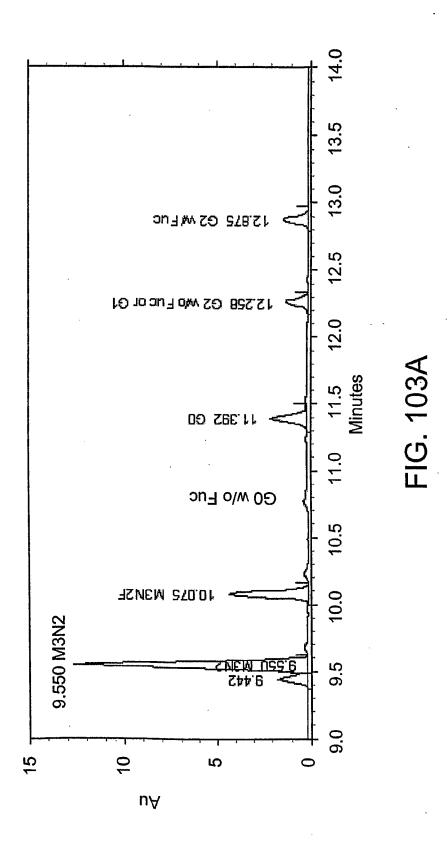
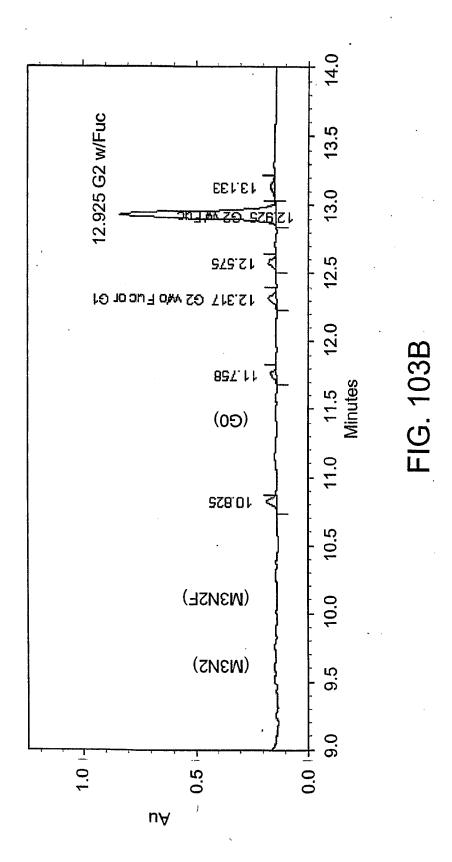
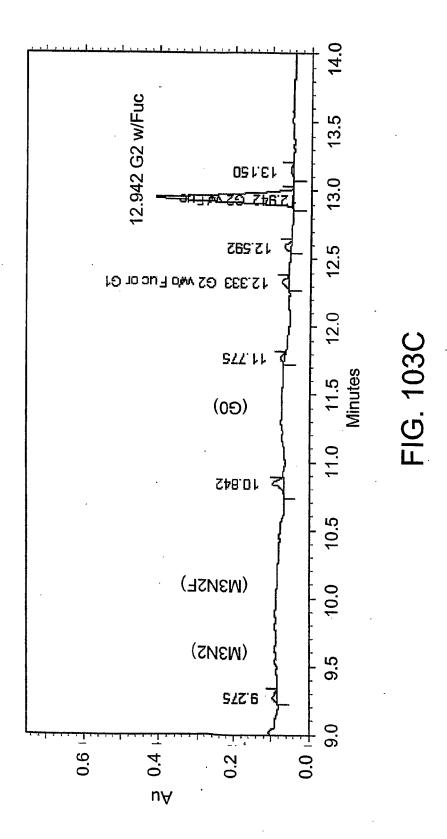
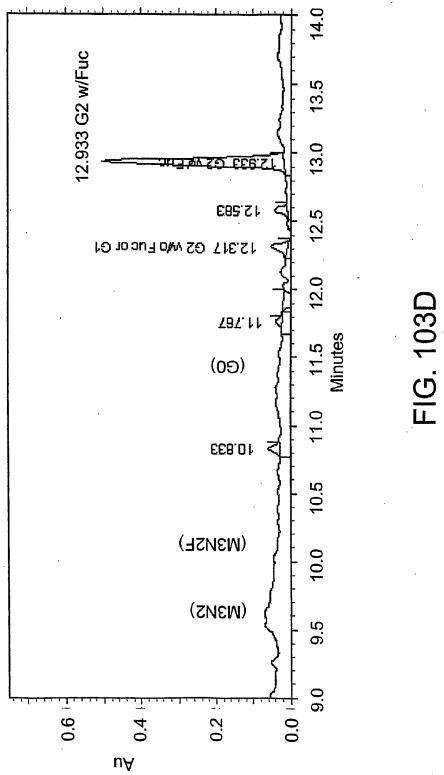


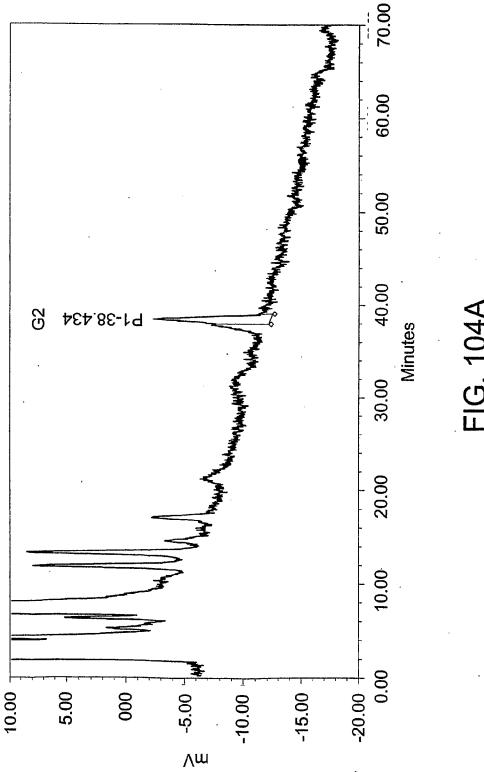
FIG. 102C











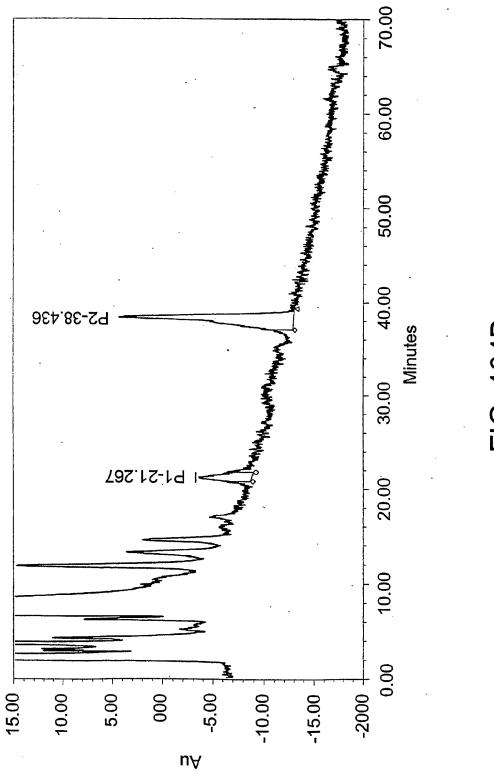
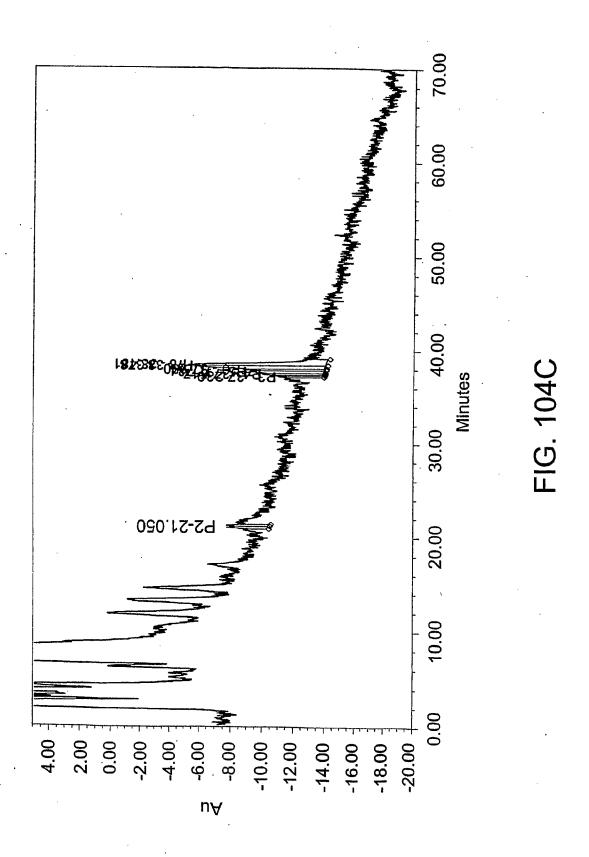


FIG. 104B



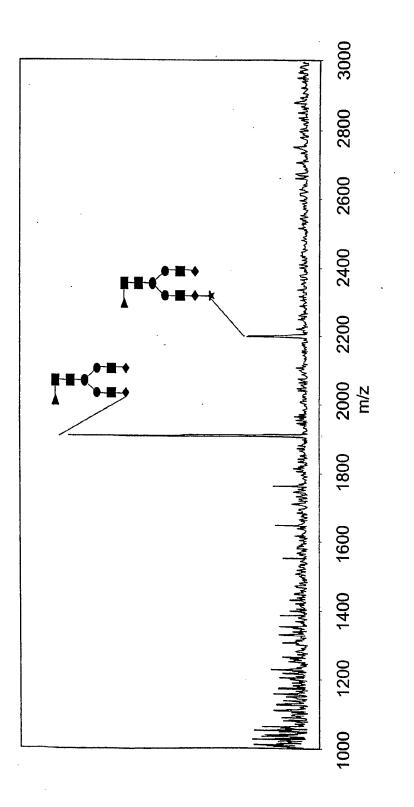


FIG. 105A

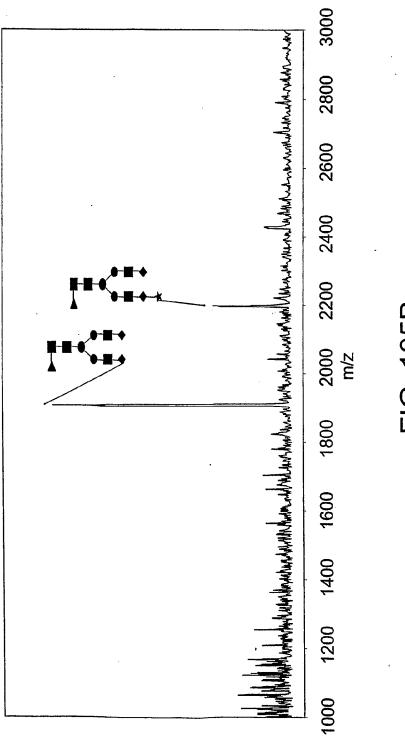


FIG. 105B

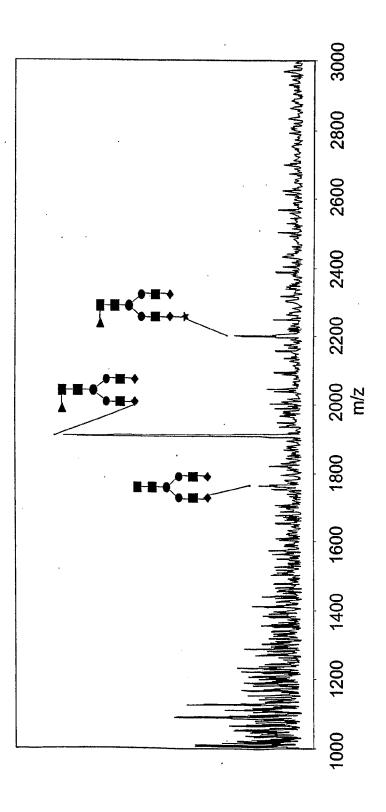
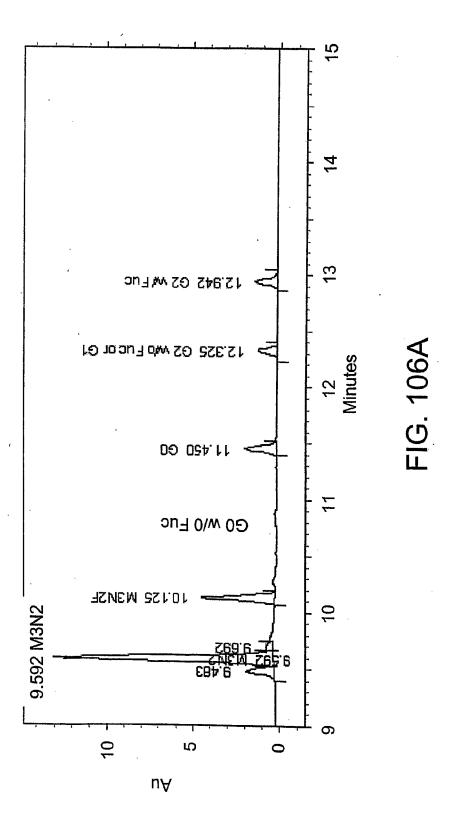
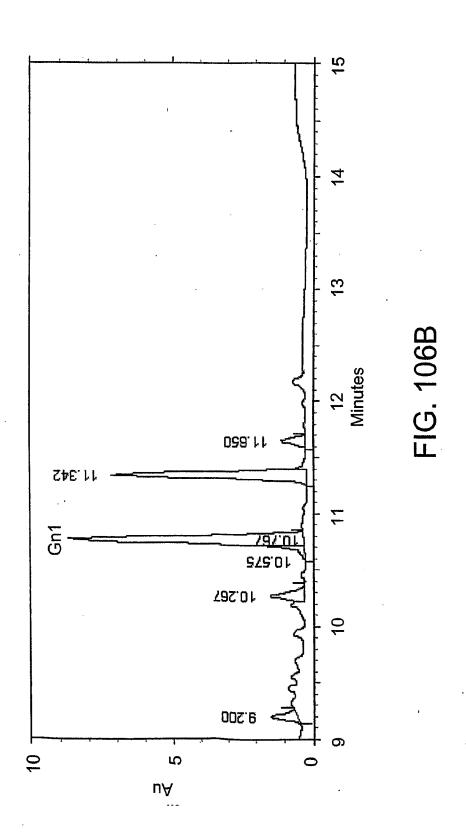
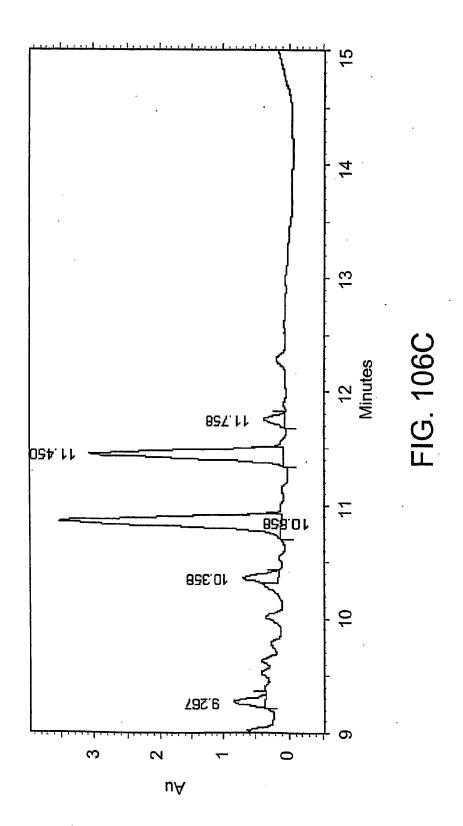
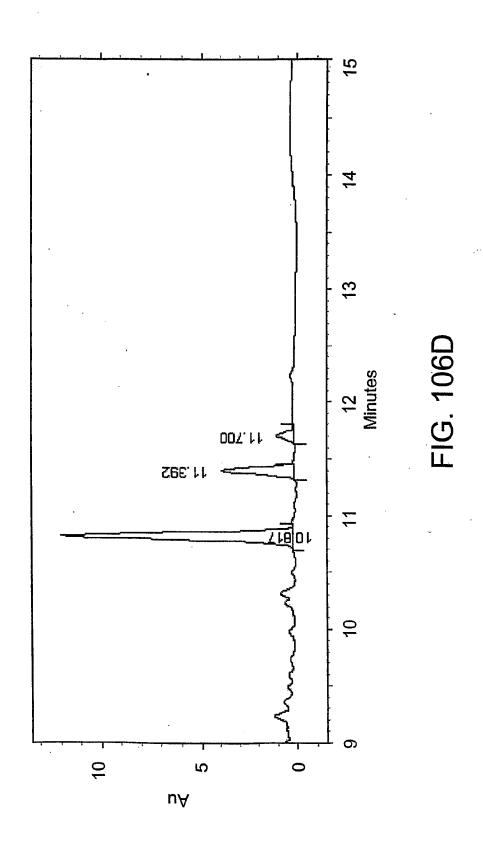


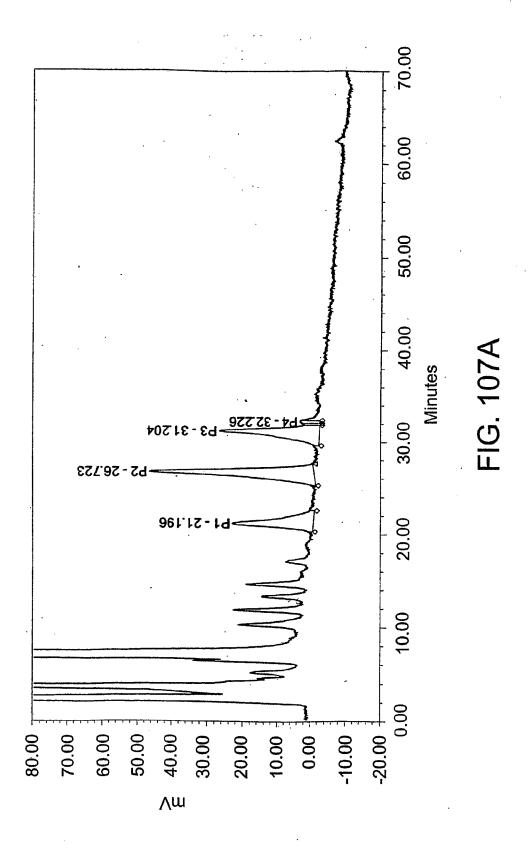
FIG. 105C

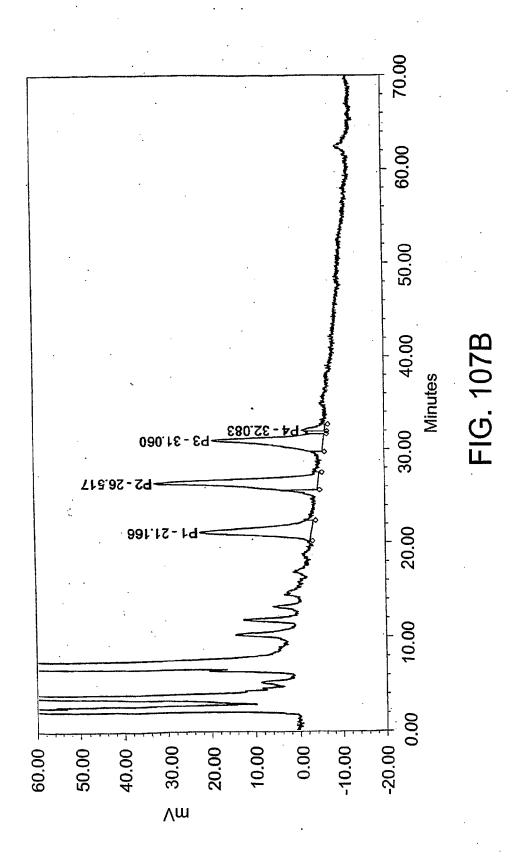


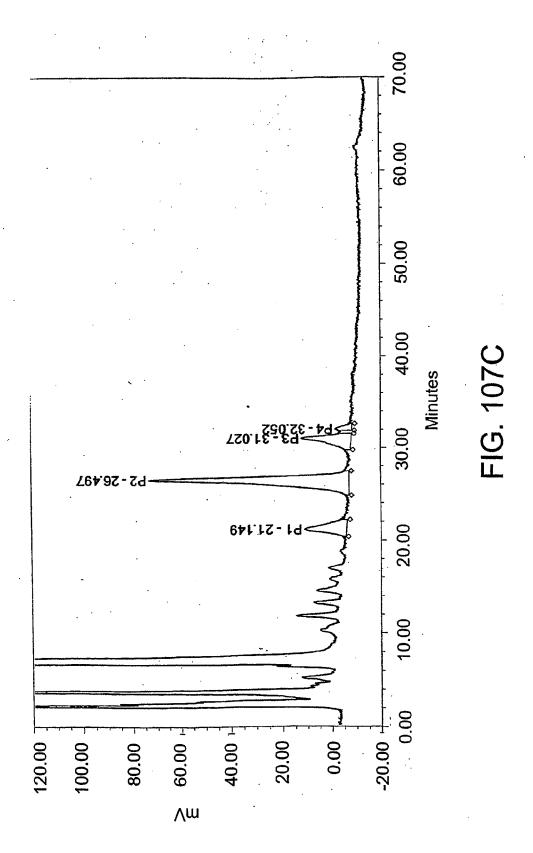


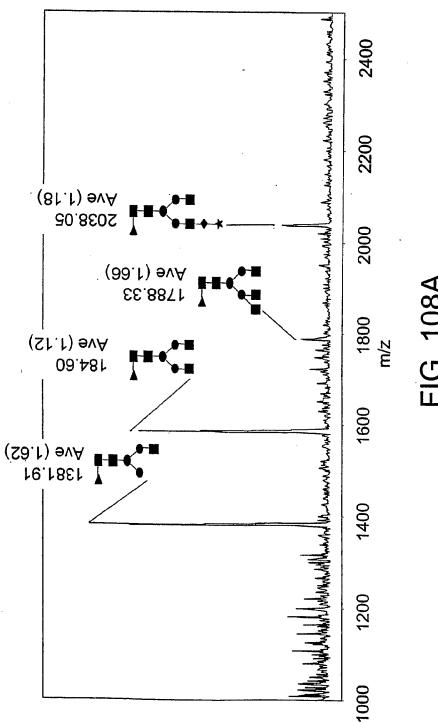


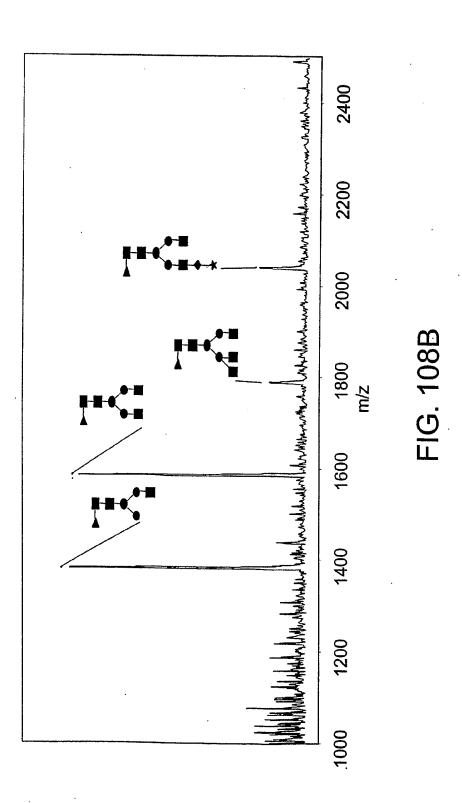


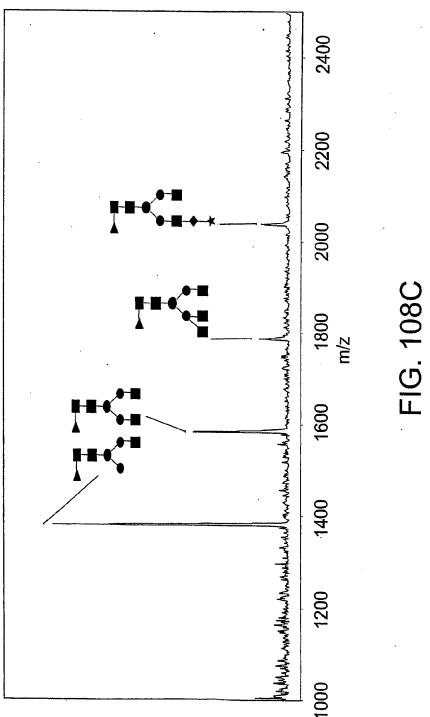


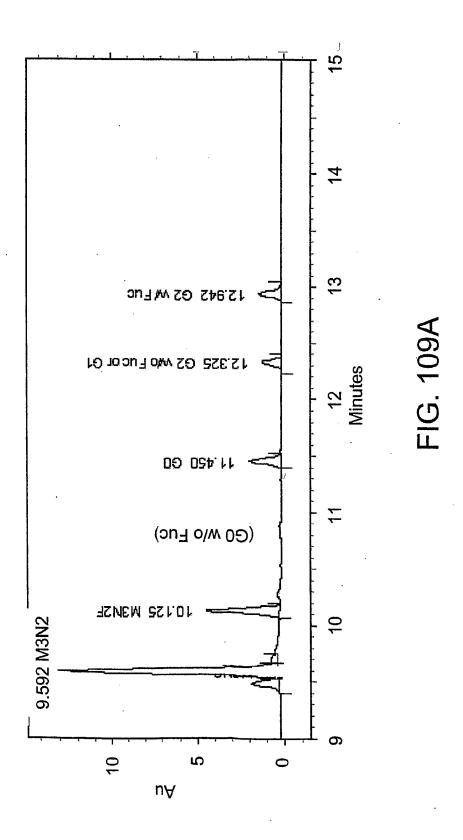


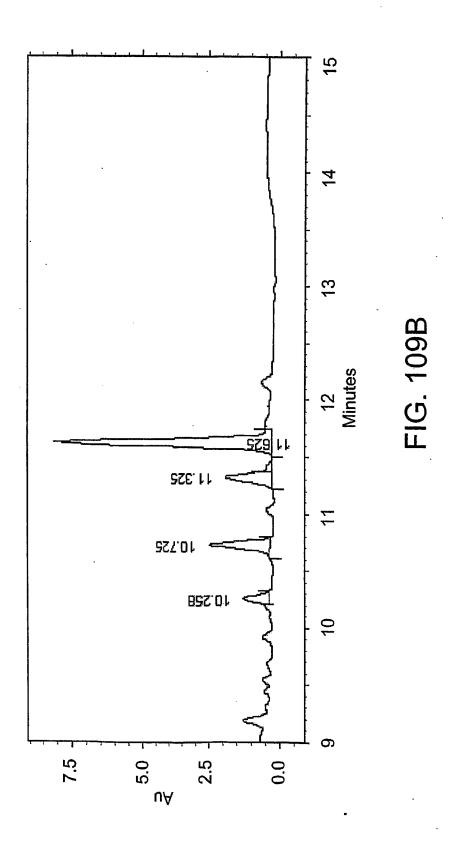


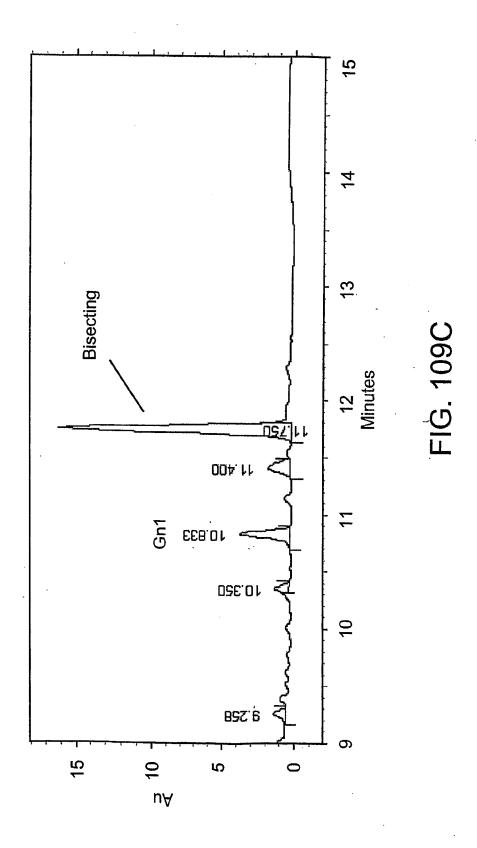


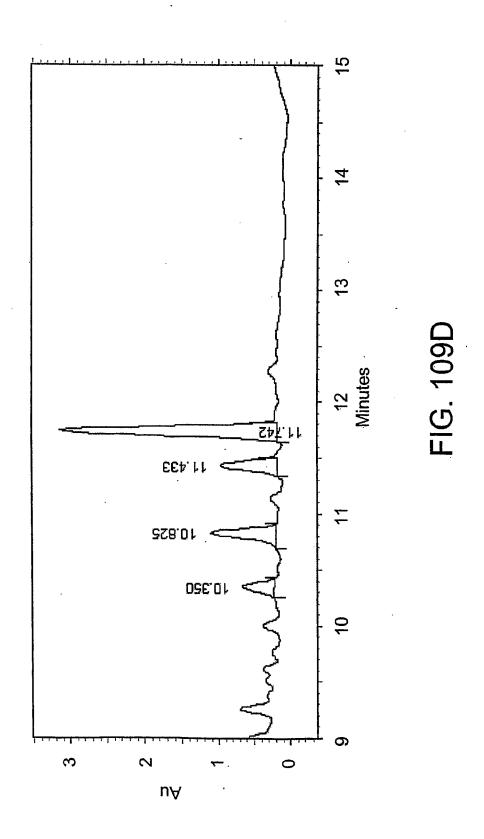


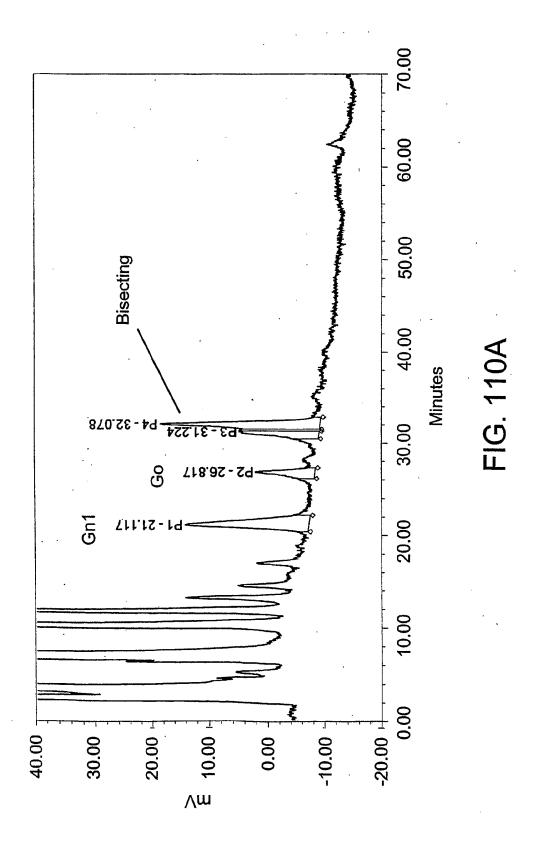


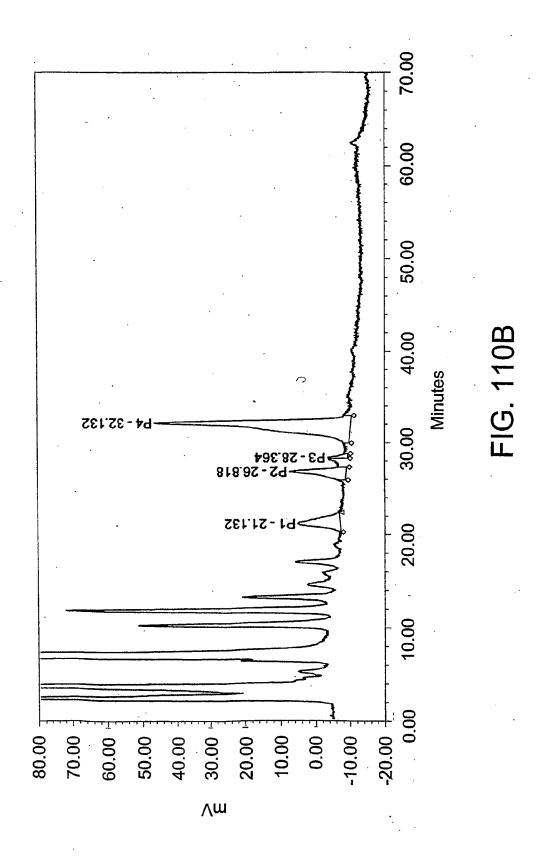


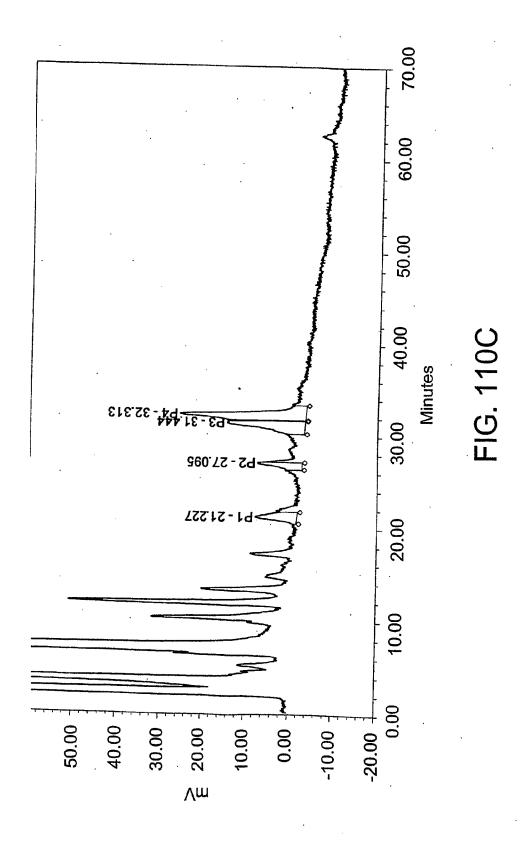












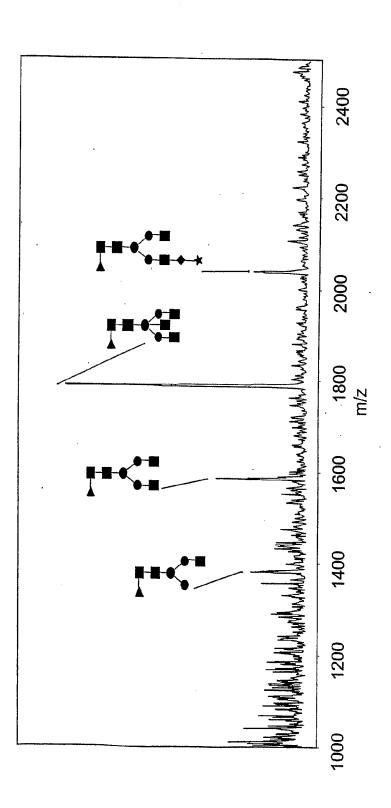
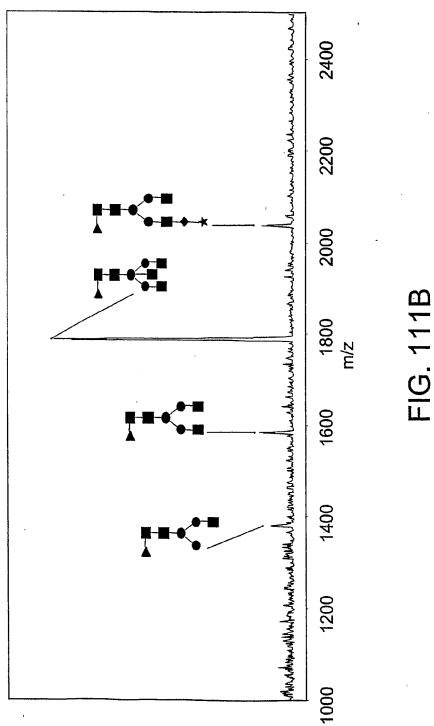
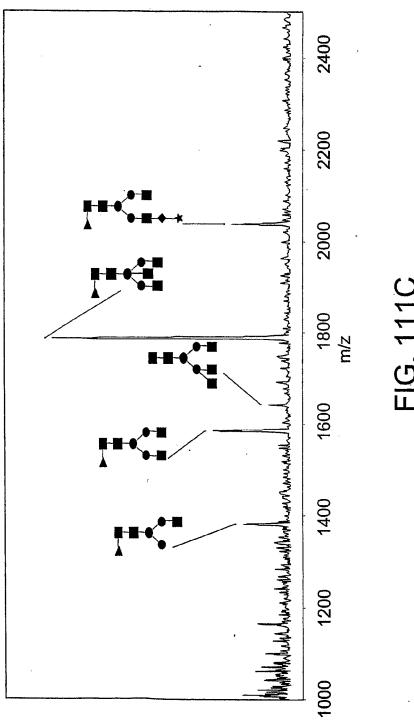


FIG. 111A





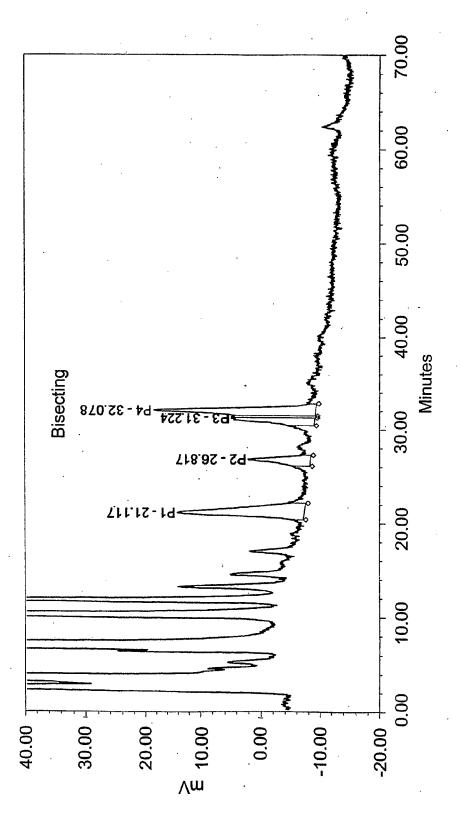
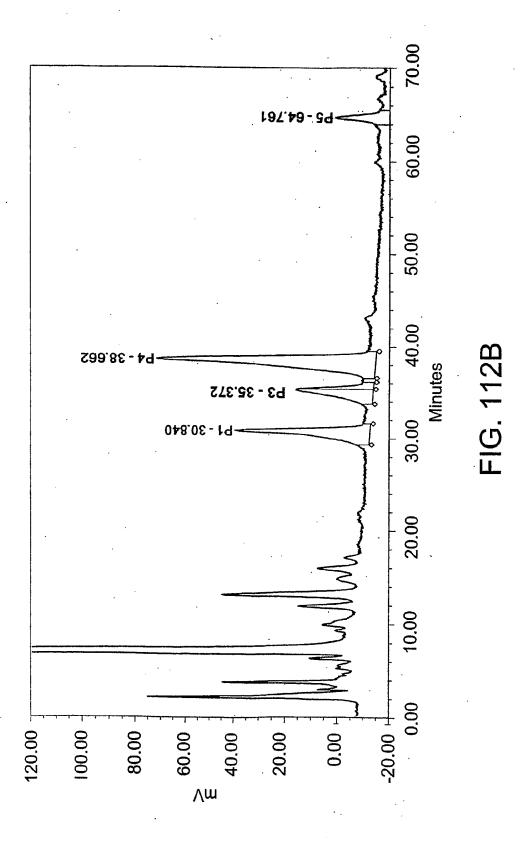
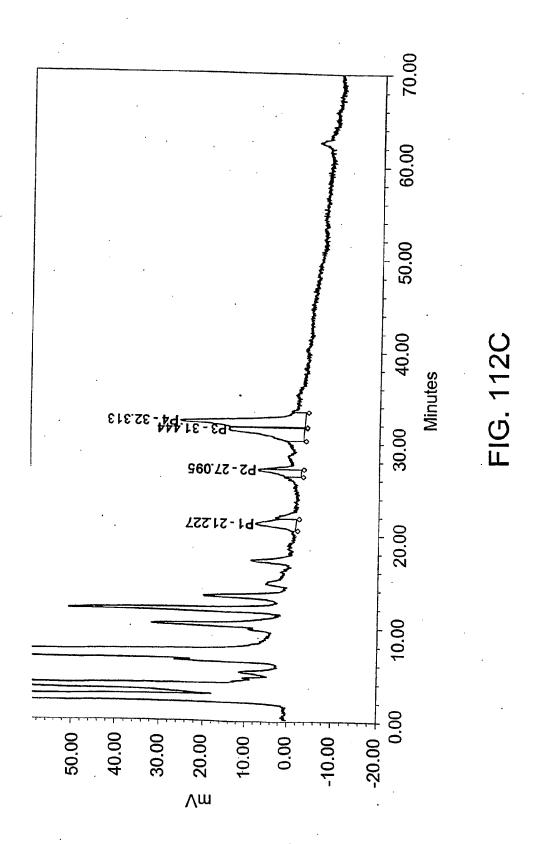
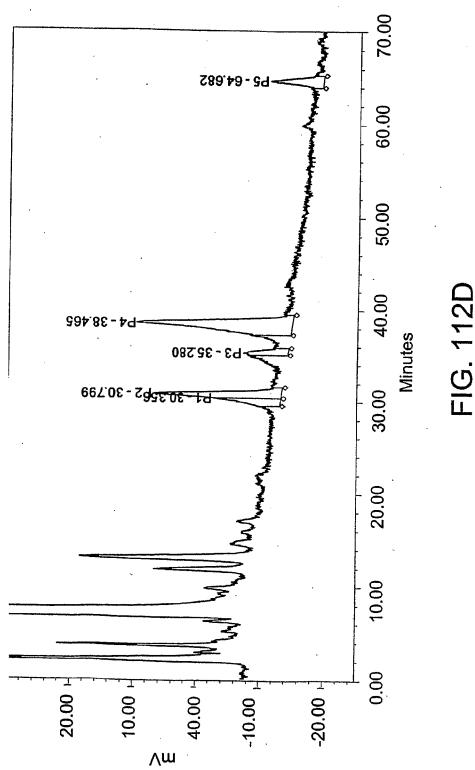


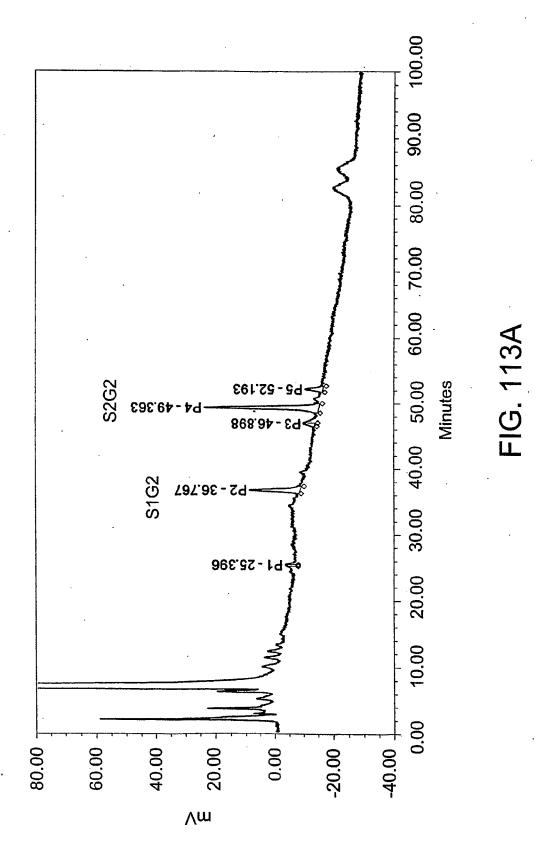
FIG. 112A

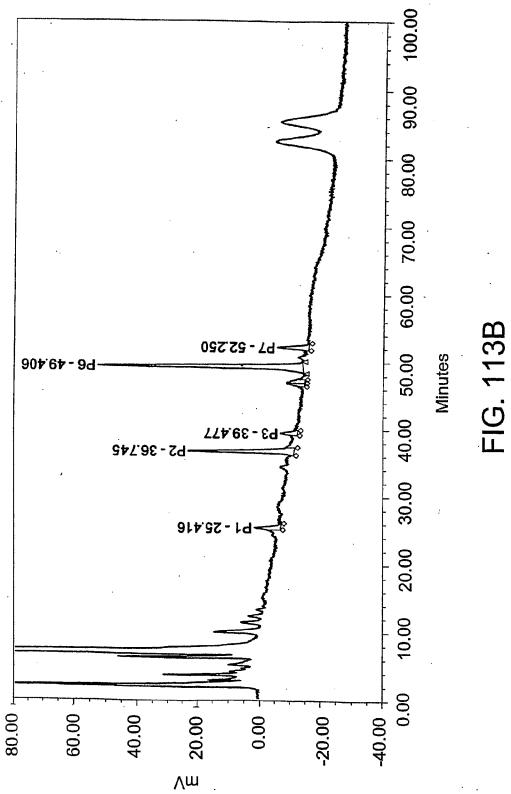


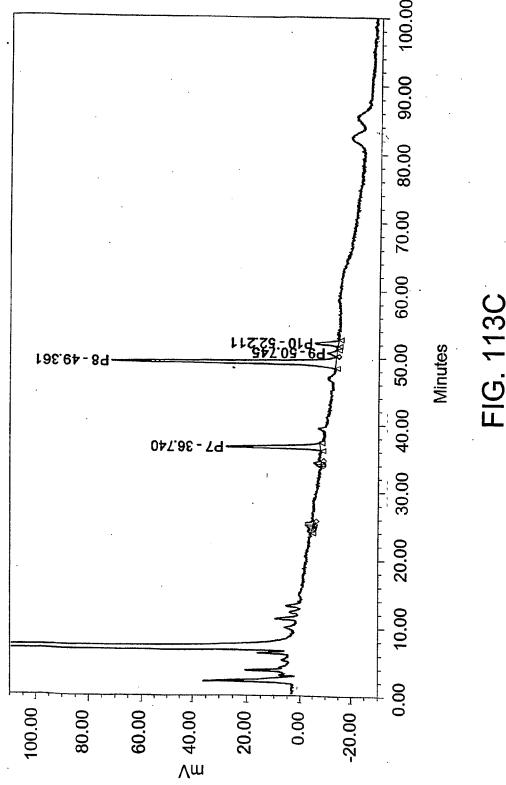
395/498

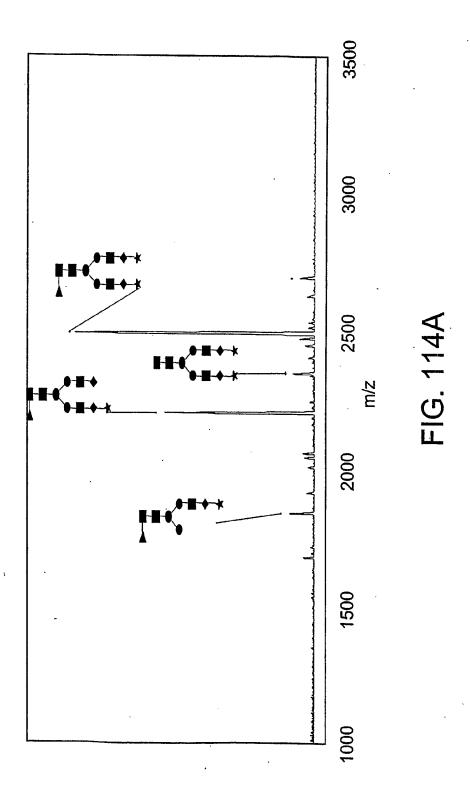


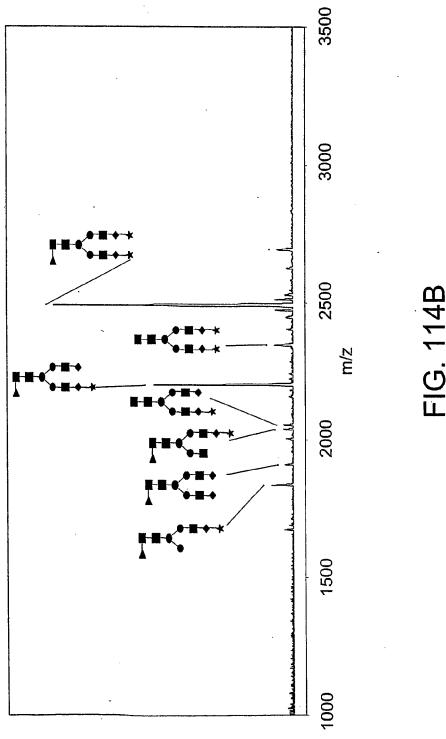


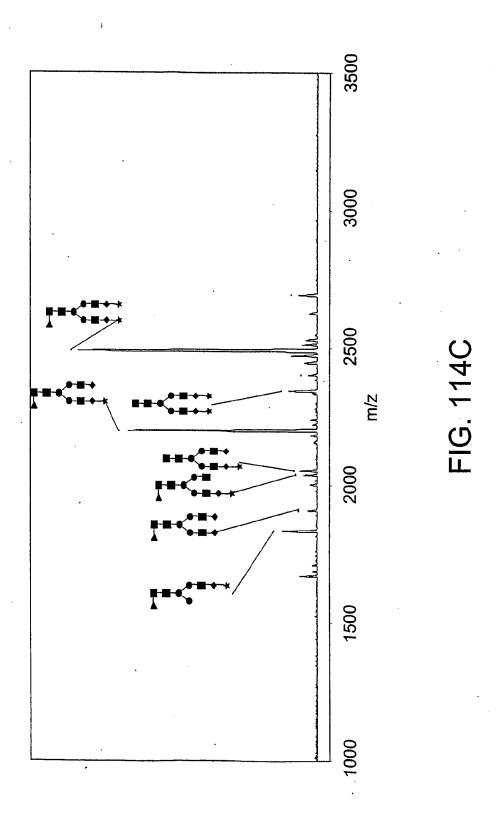












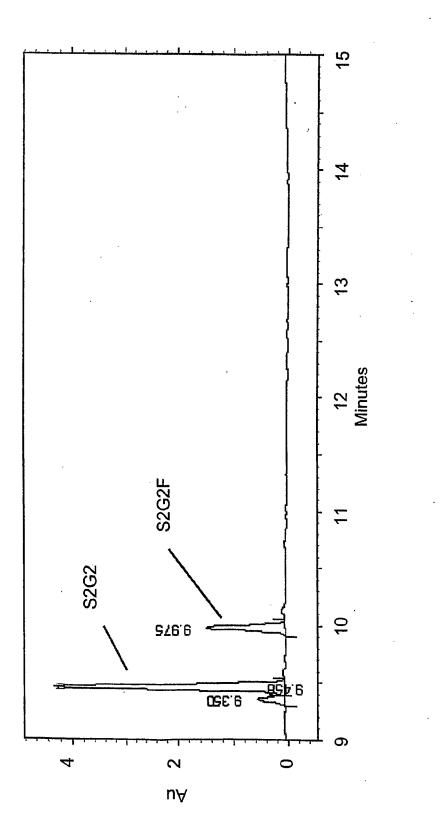
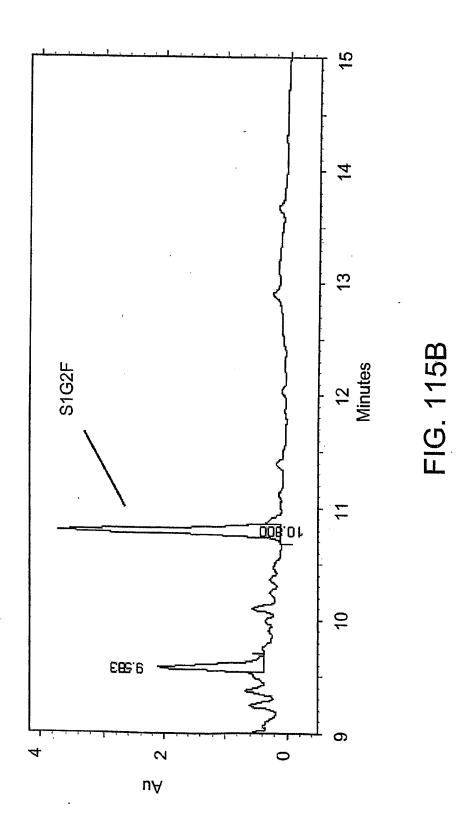
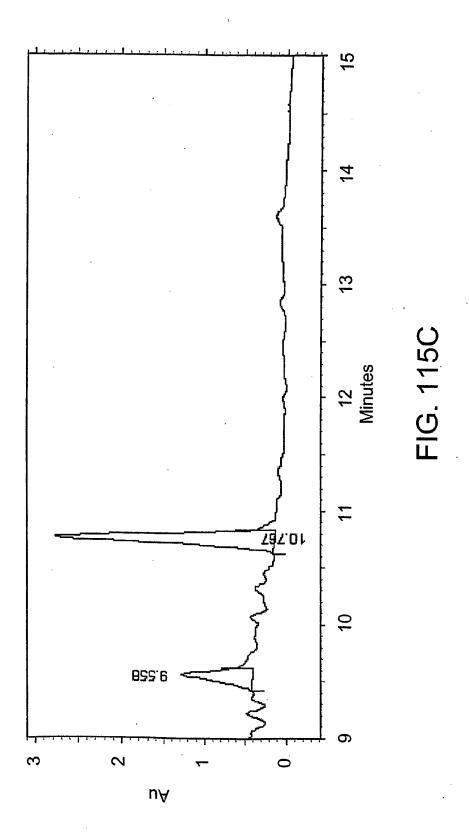
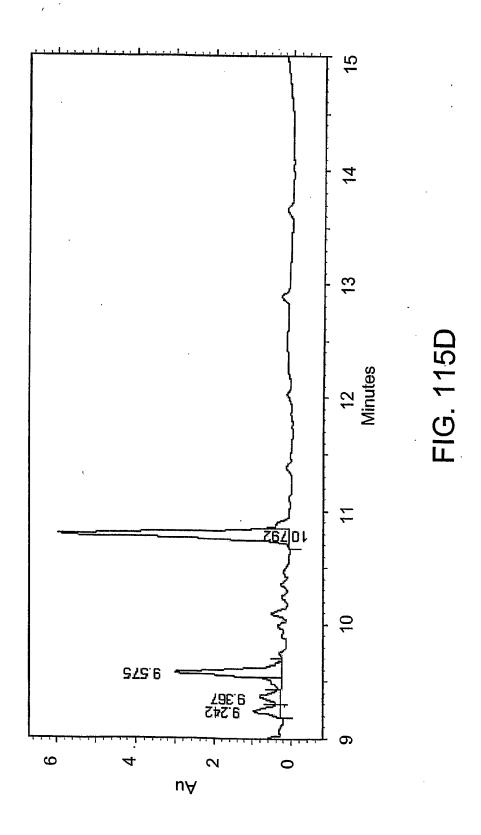


FIG. 115A

WO 2004/033651 PCT/US2003/031974







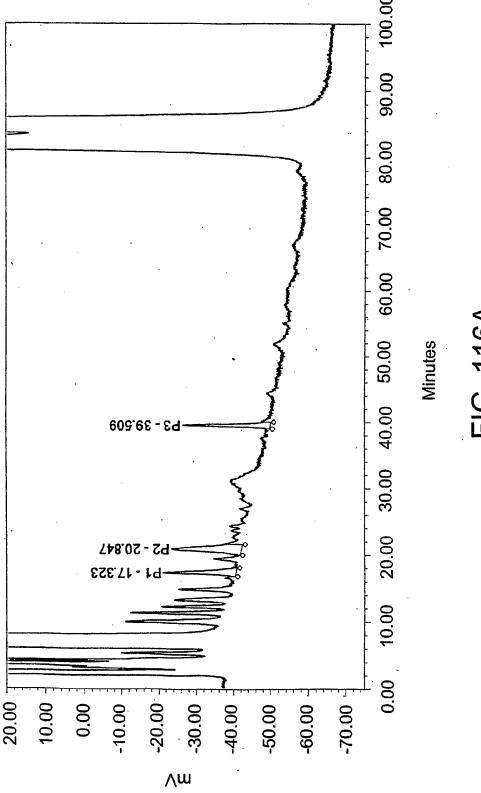
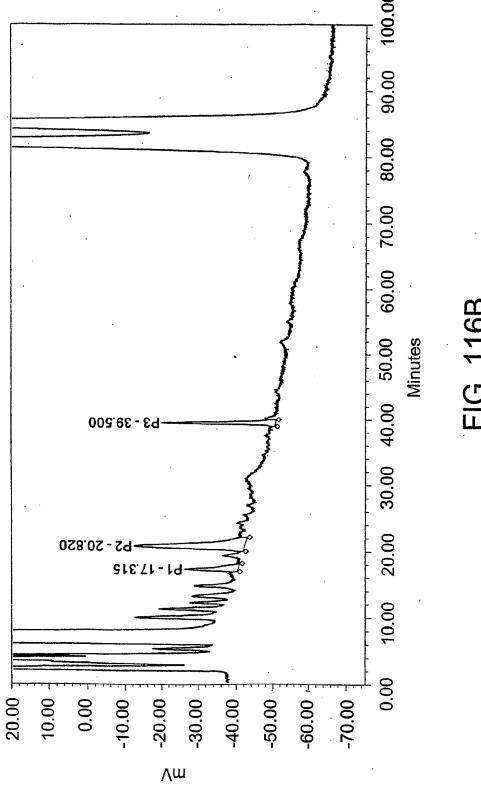
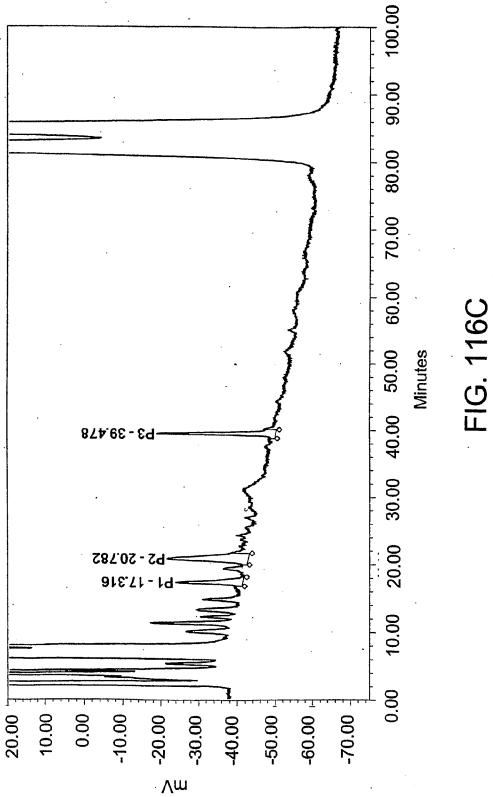


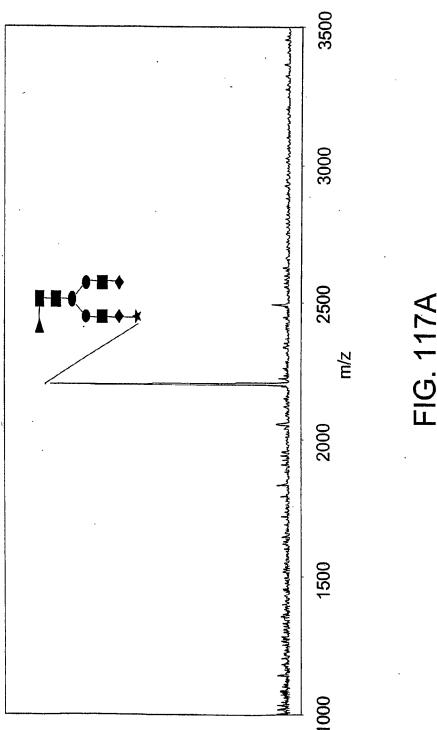
FIG. 116A

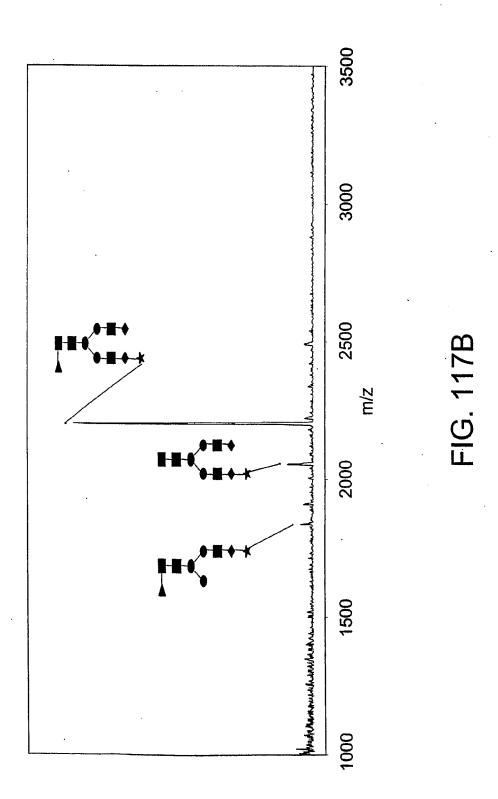




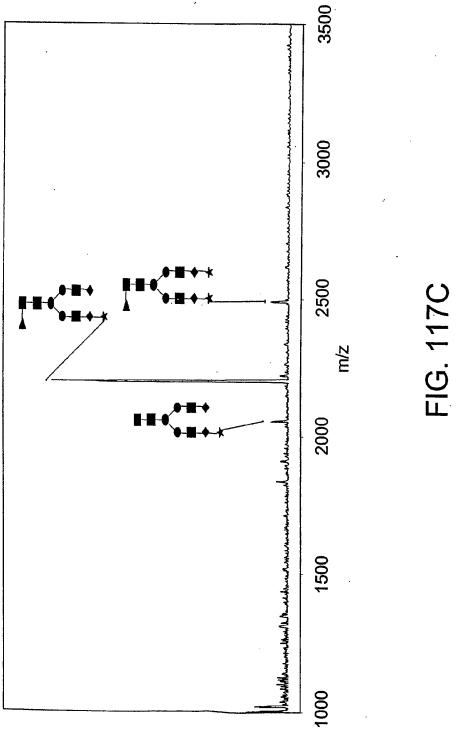


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FIG. 118B

FIG. 118A

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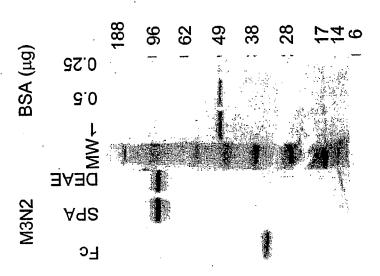


FIG. 118D

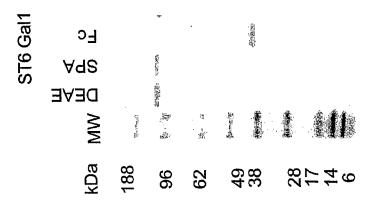


FIG. 118C

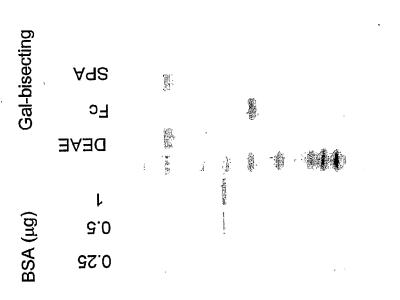
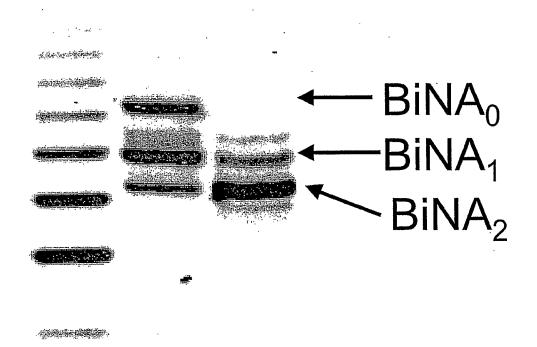


FIG. 118E

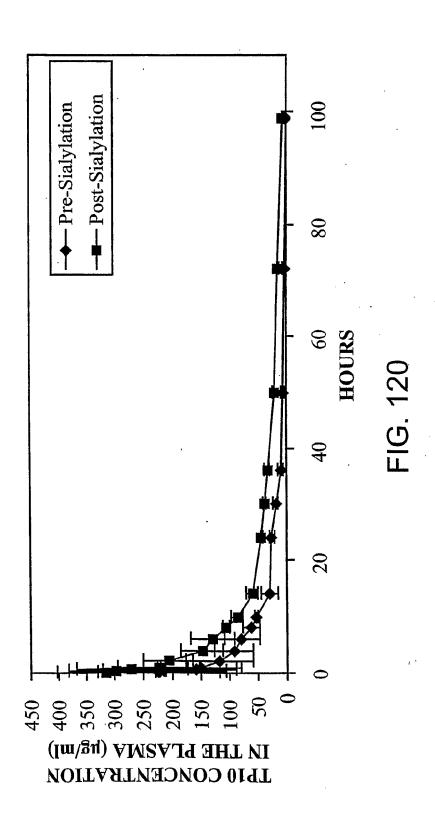
WO 2004/033651 PCT/US2003/031974

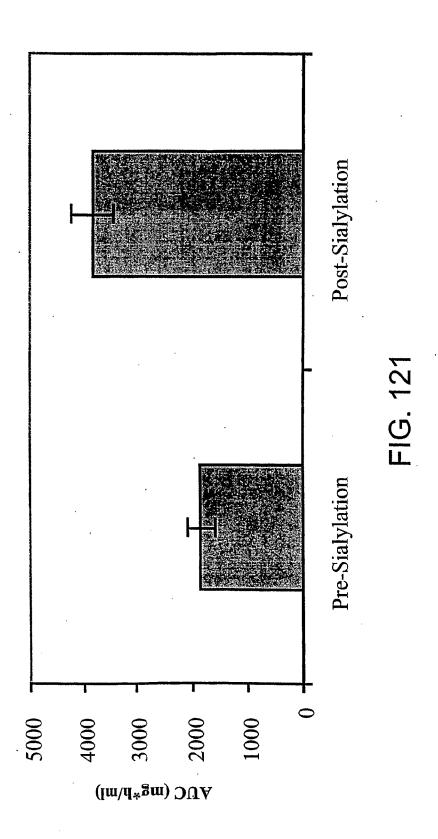
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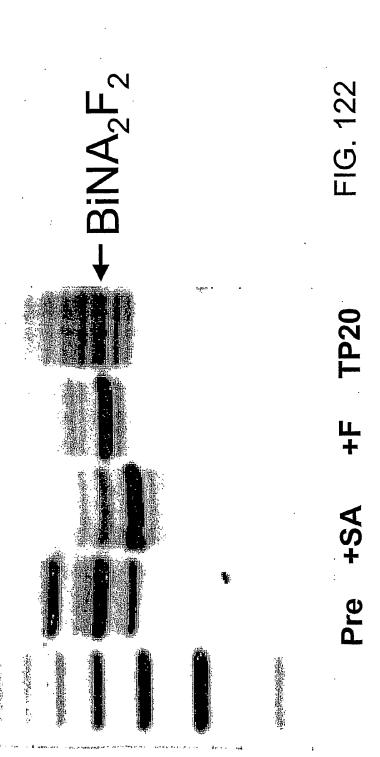
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FIG. 119

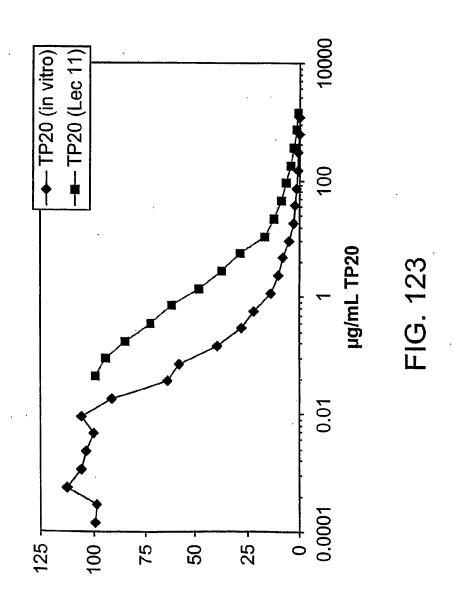


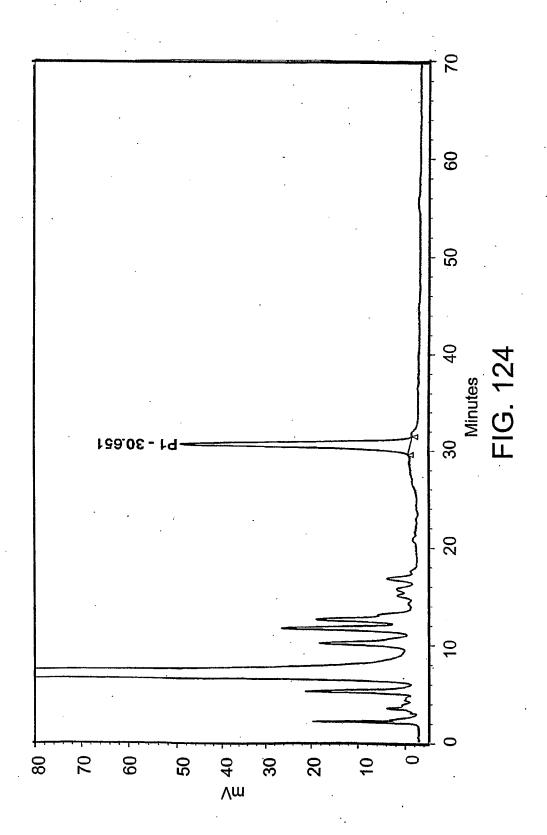


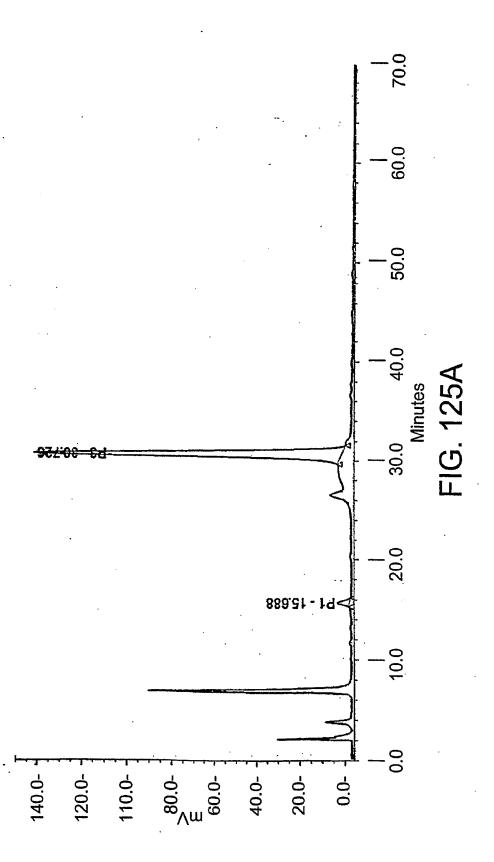
WO 2004/033651 PCT/US2003/031974

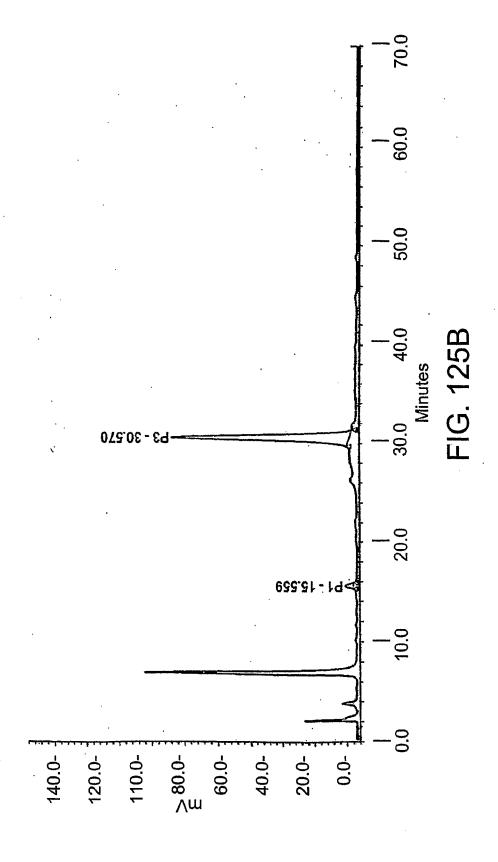


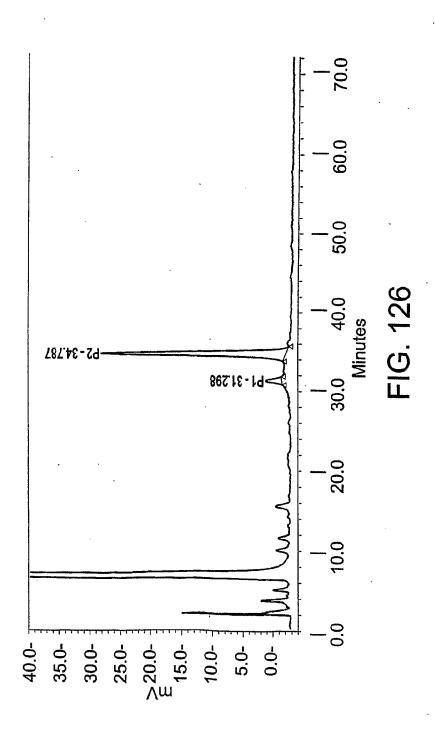
WO 2004/033651 PCT/US2003/031974



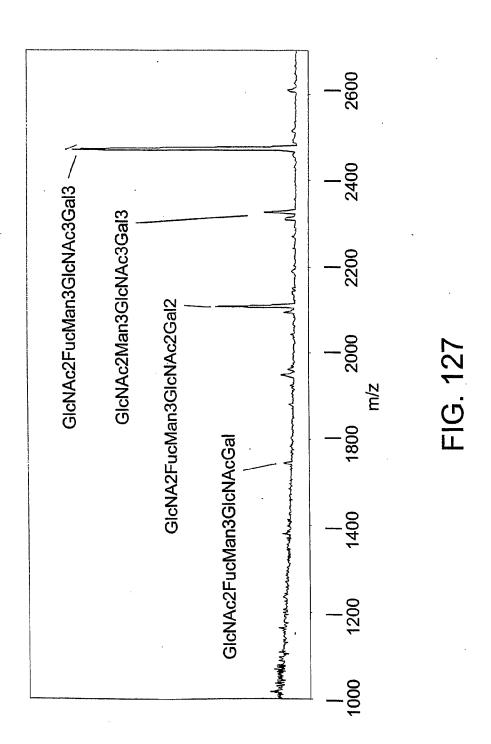


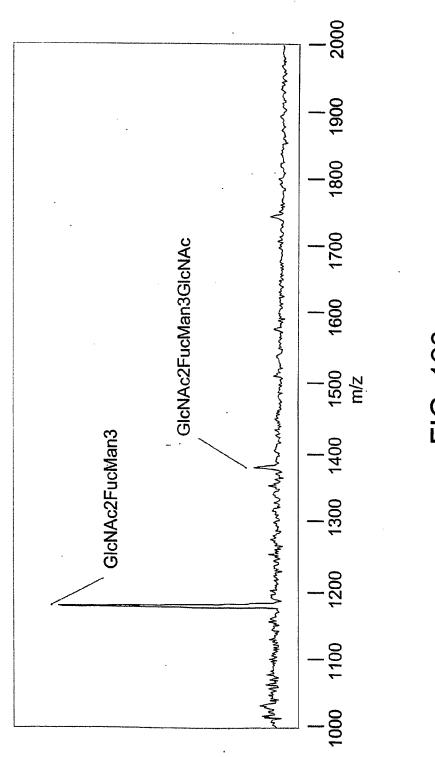






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-1G. 128

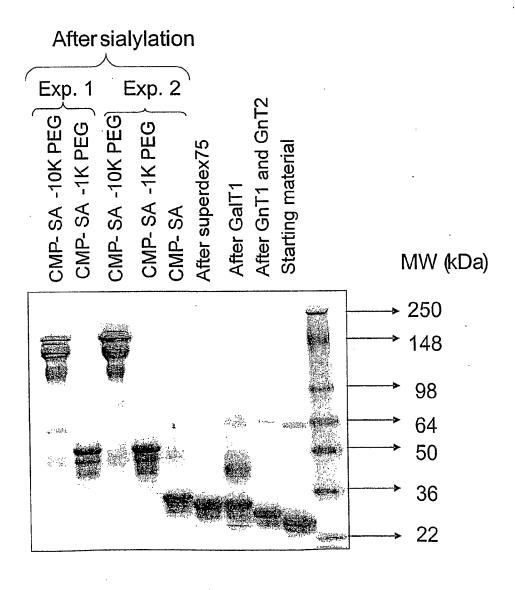
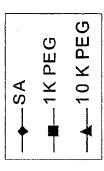


FIG. 129



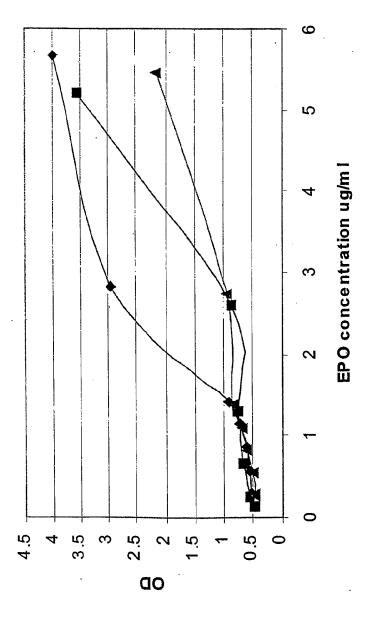
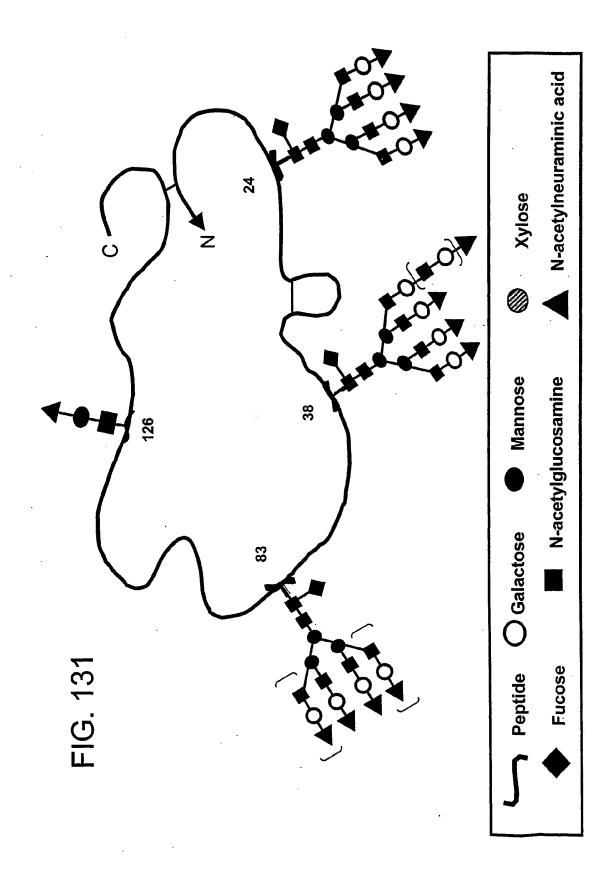
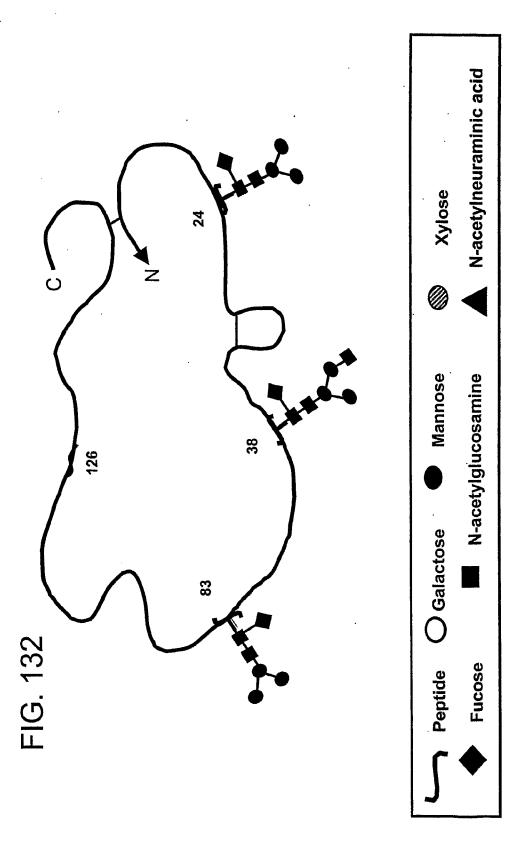


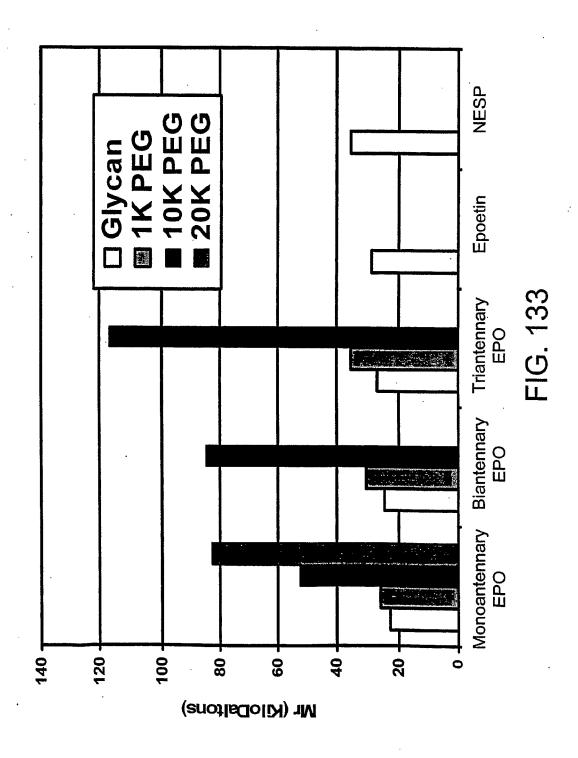
FIG. 130

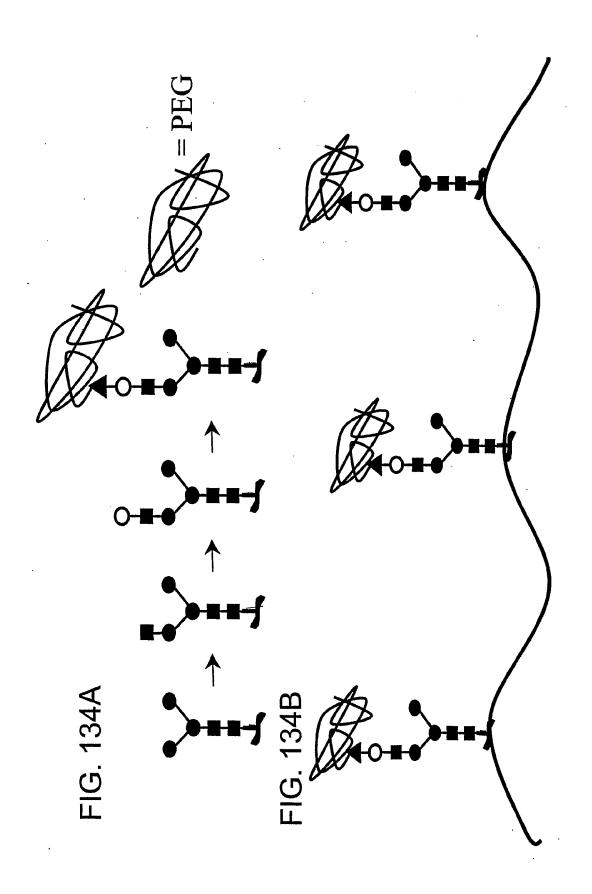
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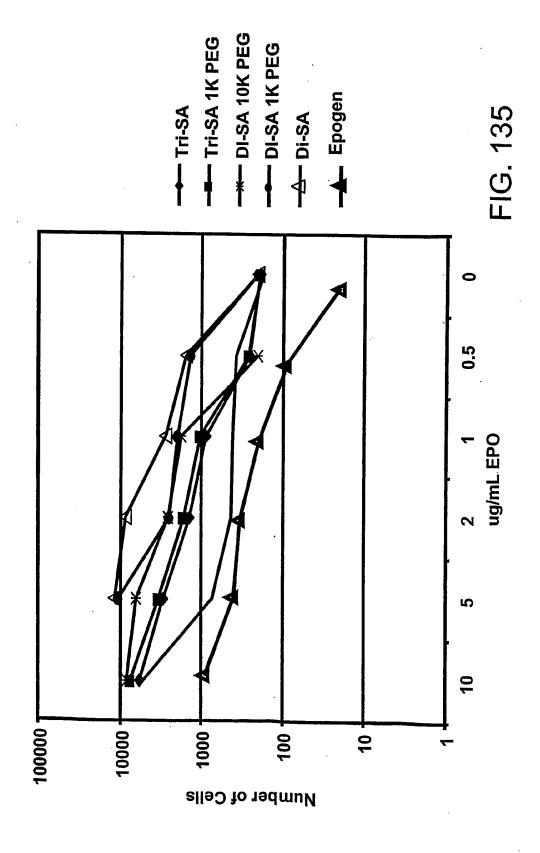


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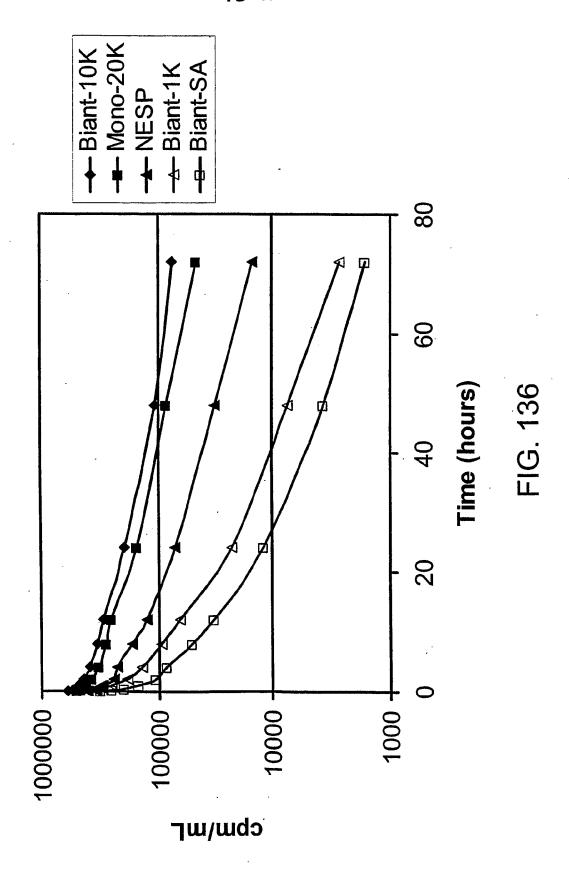








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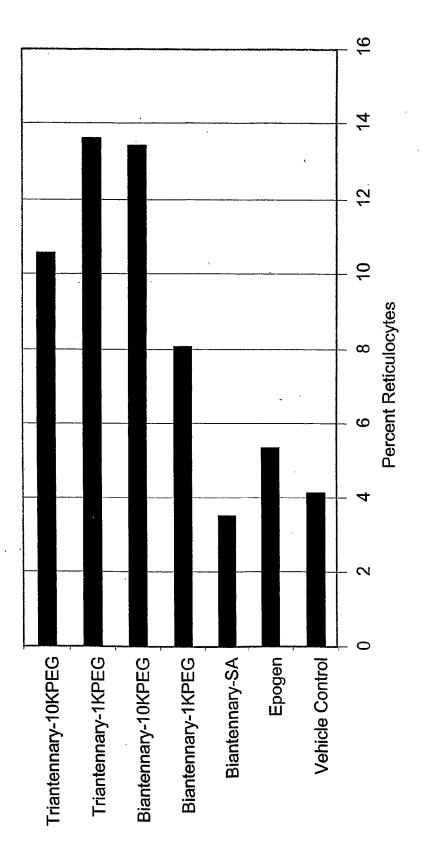


FIG. 137

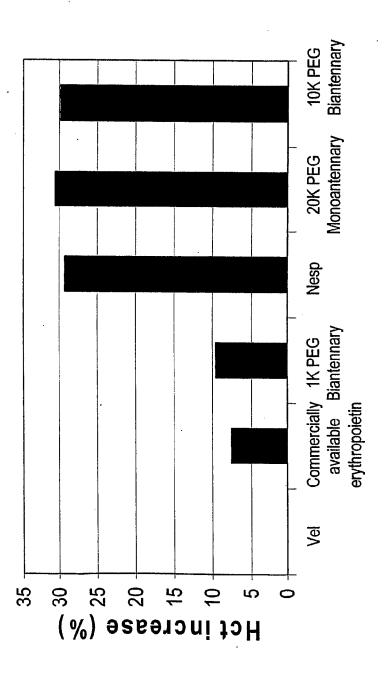
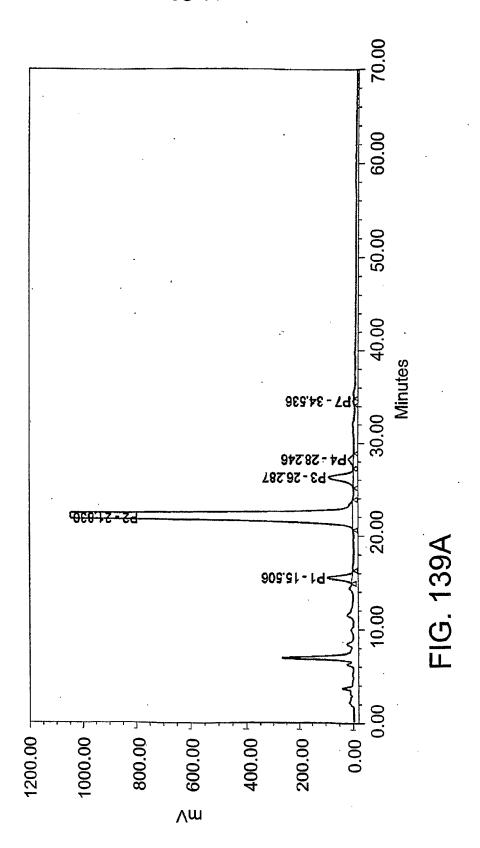
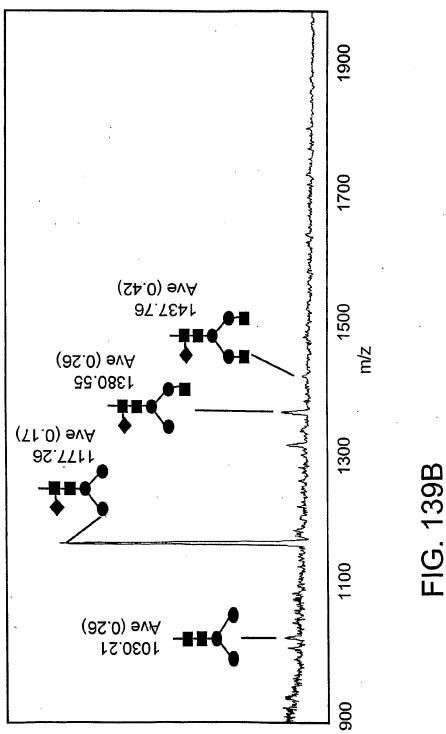
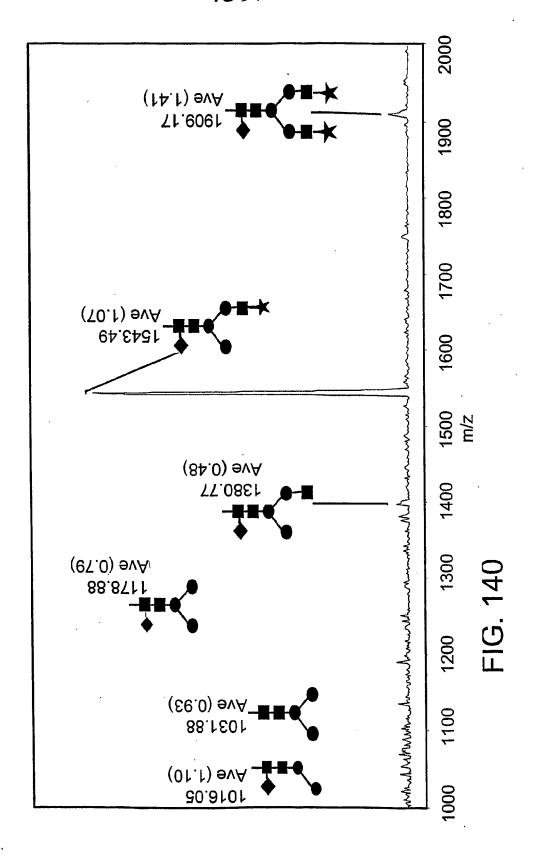


FIG. 138







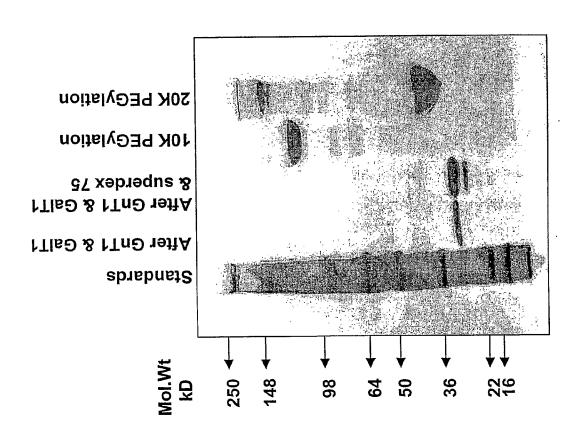
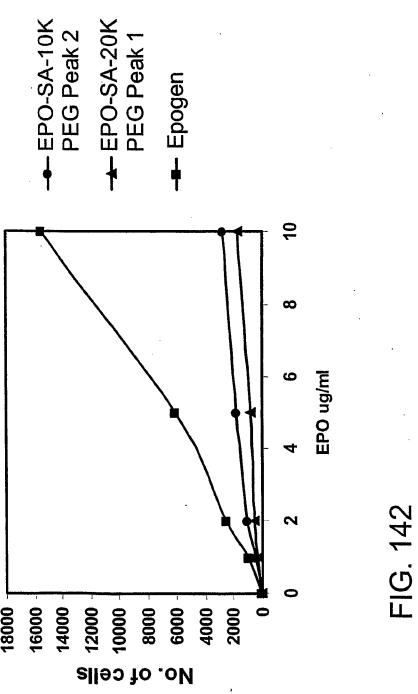


FIG. 141



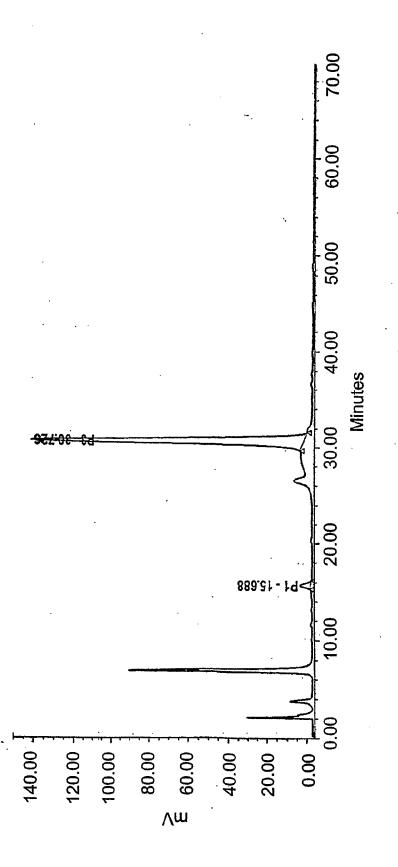


FIG. 143A

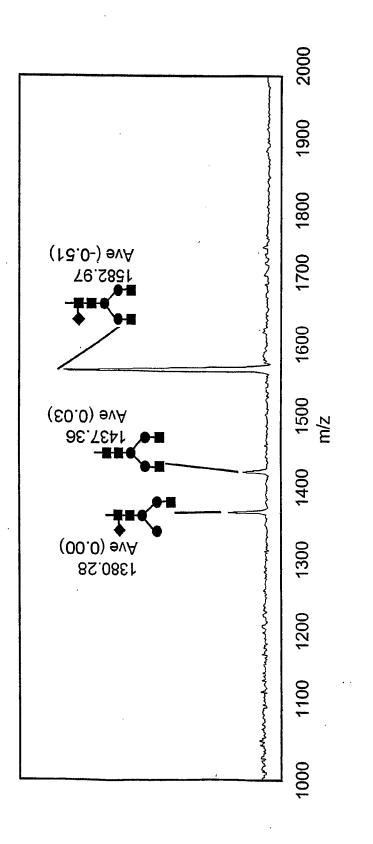
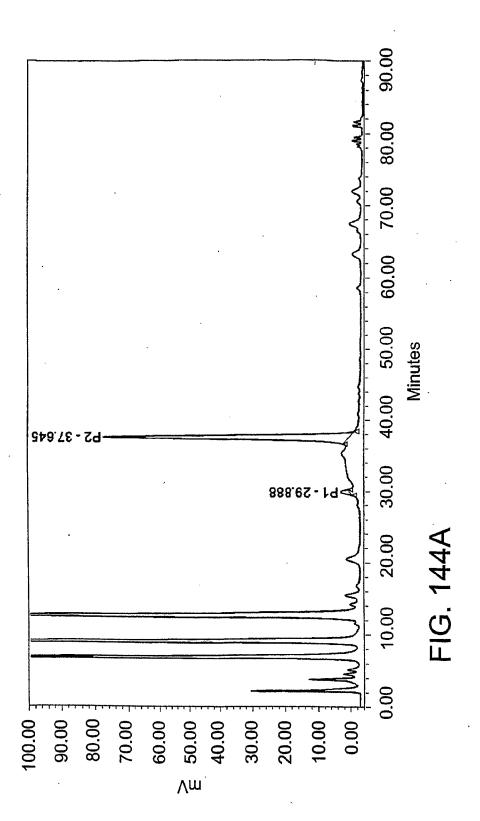
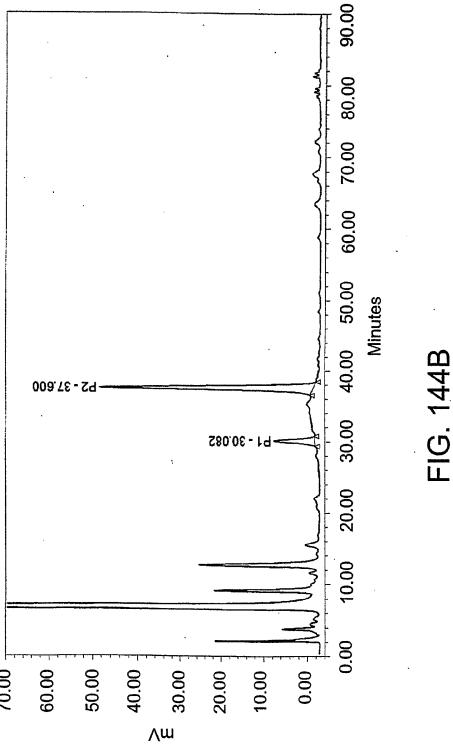


FIG. 1431





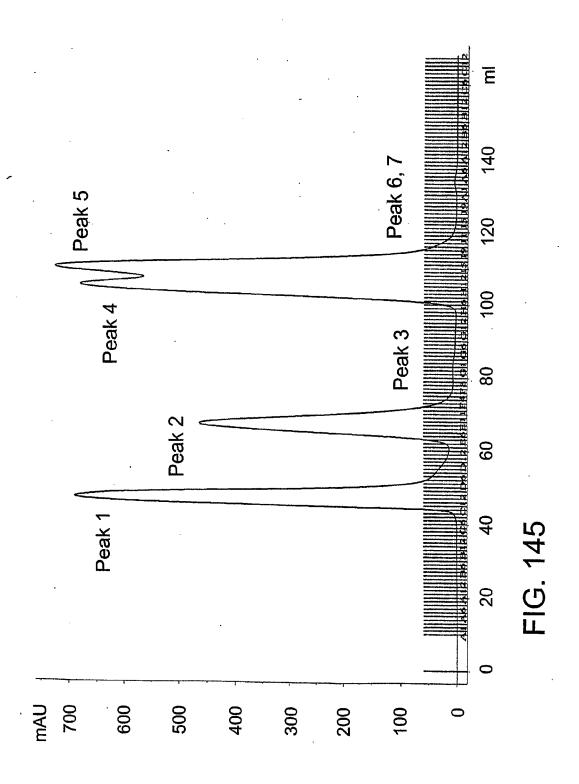
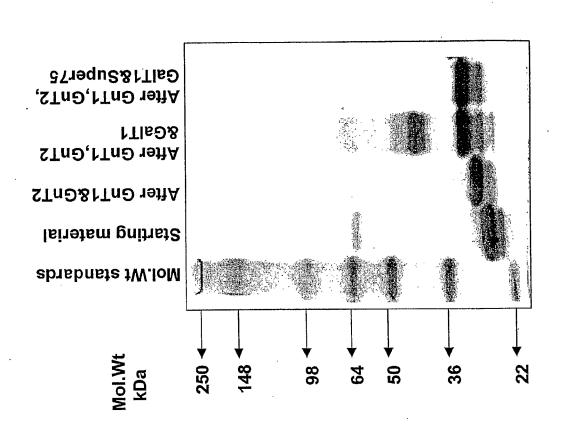
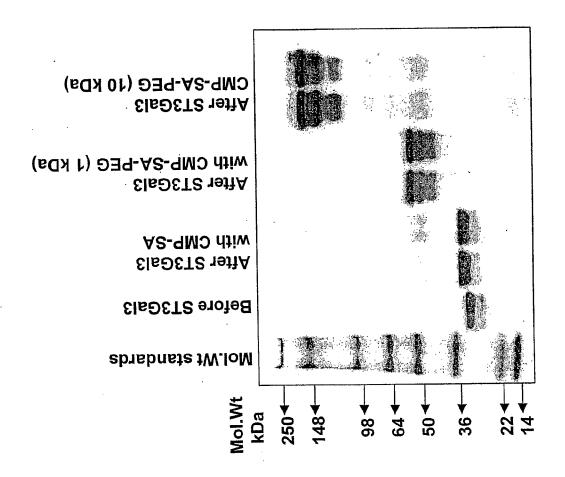
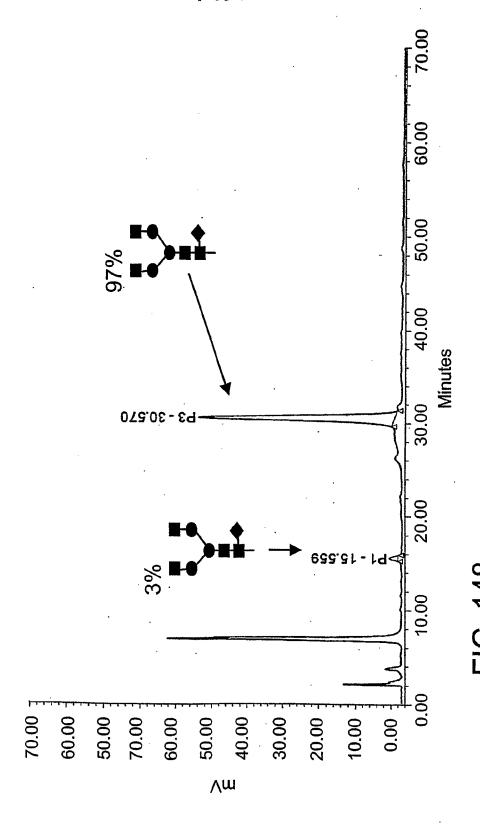


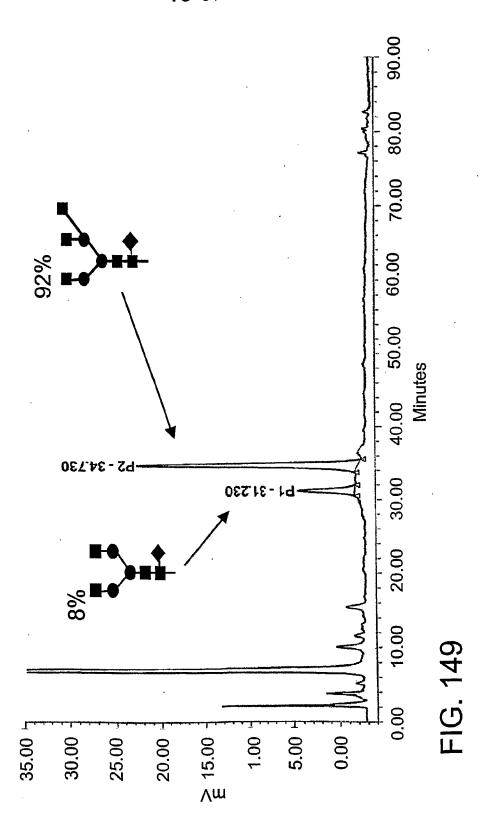
FIG. 146

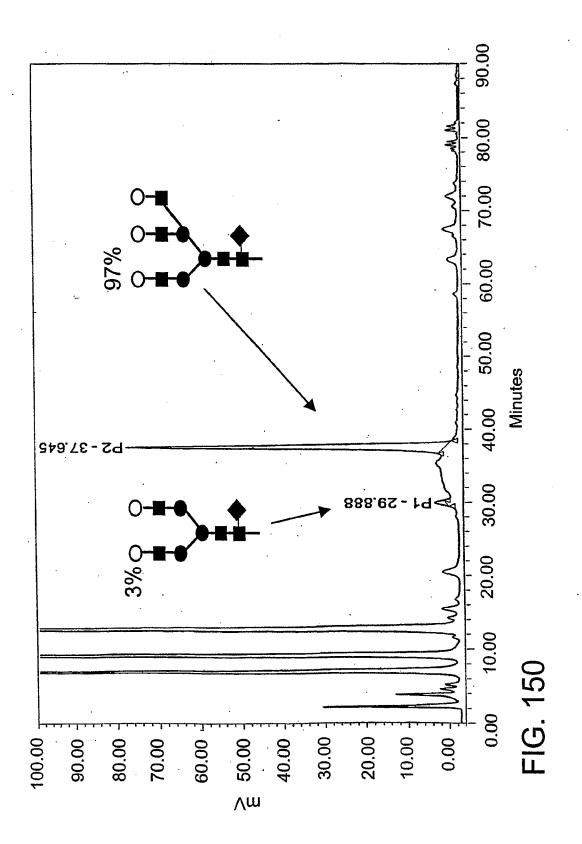


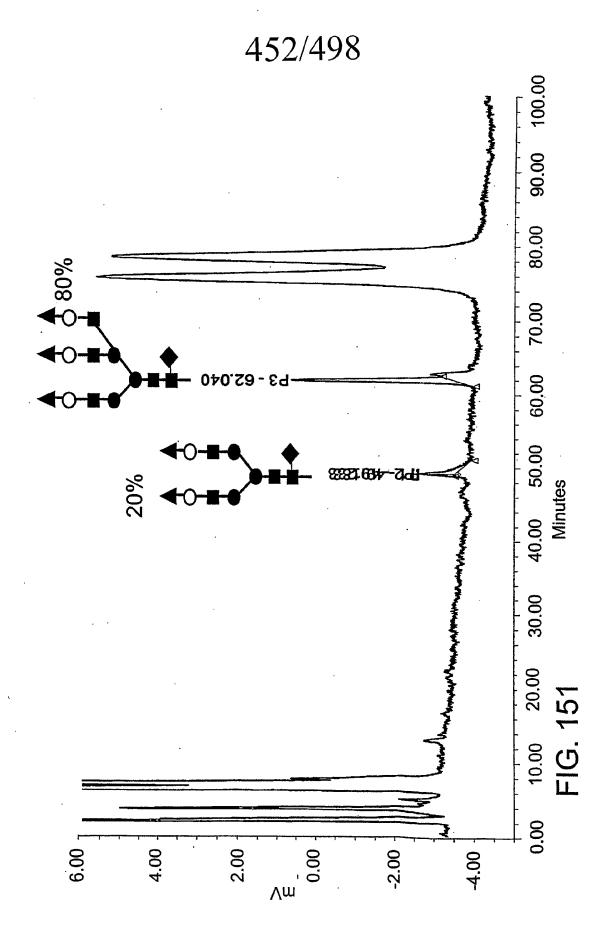


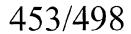
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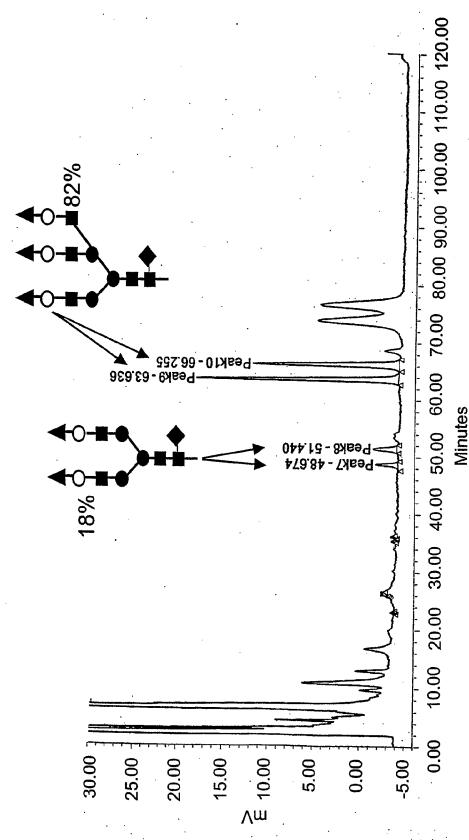
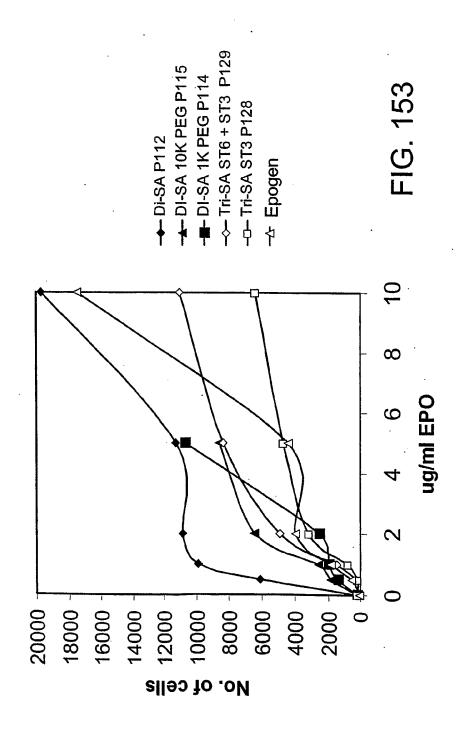


FIG. 152



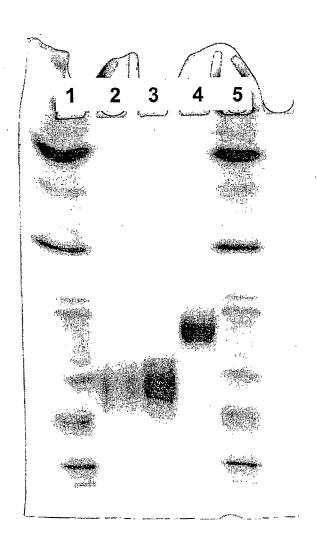


FIG. 154

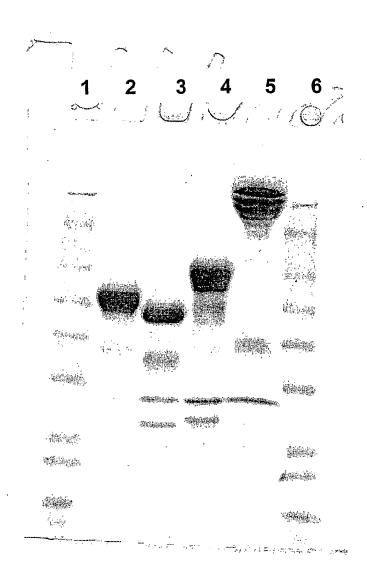


FIG. 155

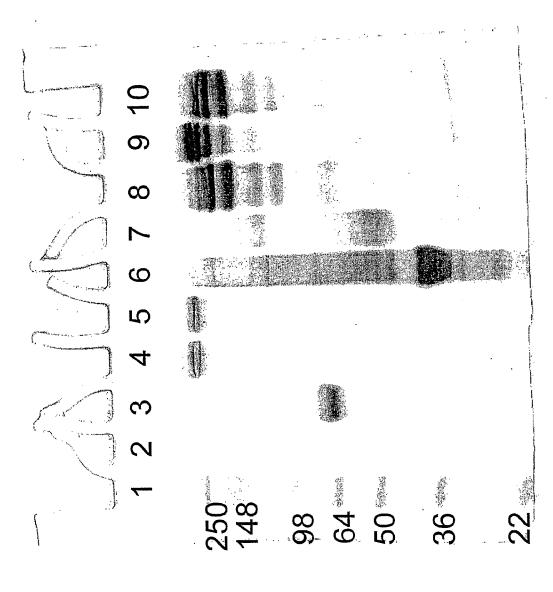


FIG. 156

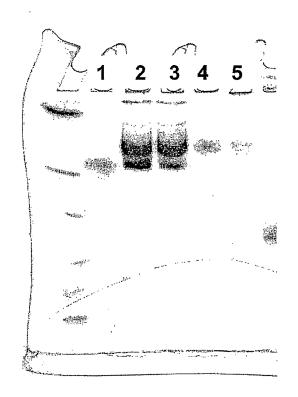
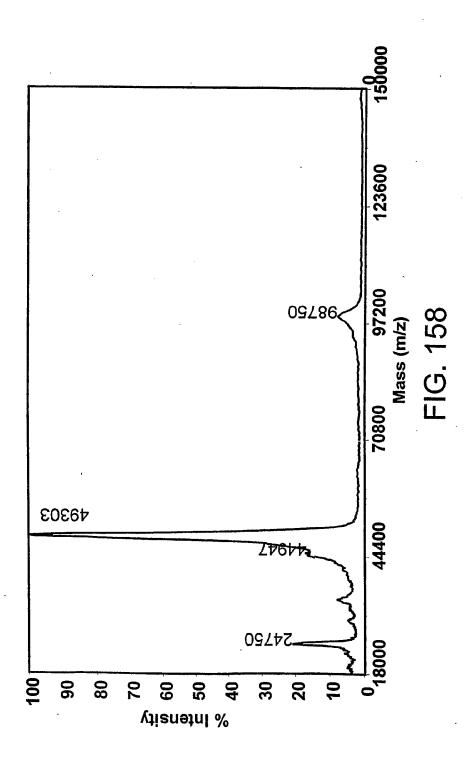
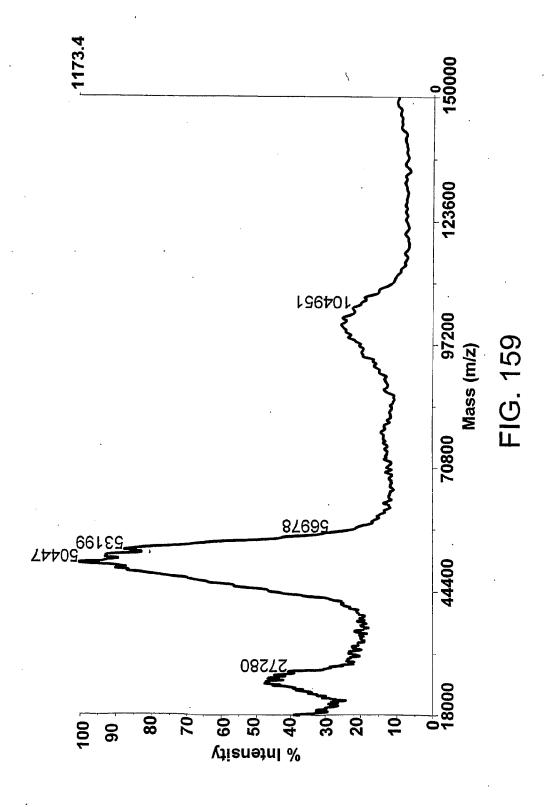
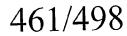


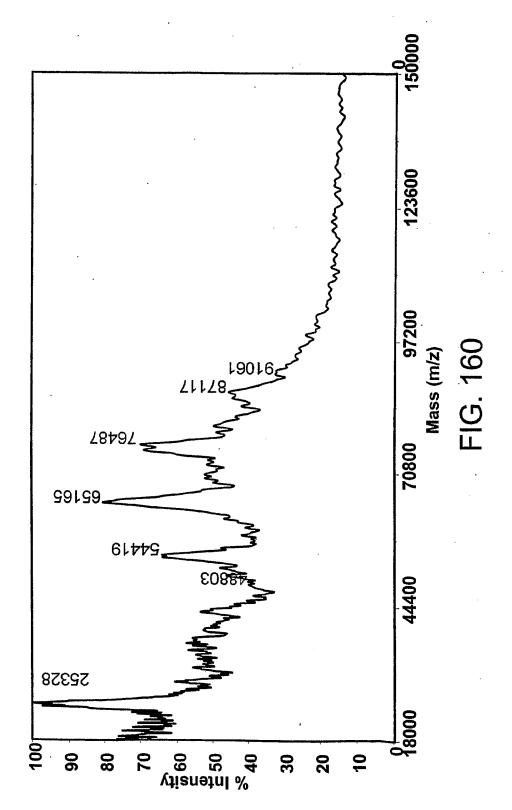
FIG. 157



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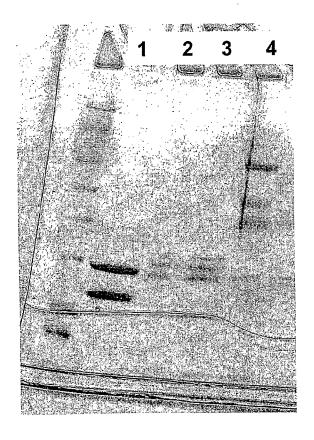


FIG. 161

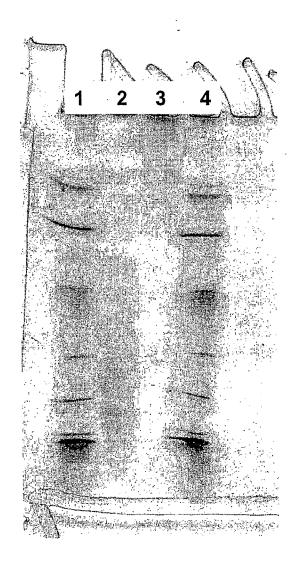


FIG. 162



FIG. 163

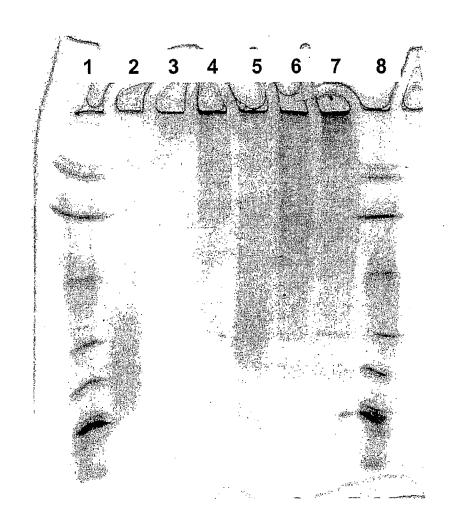


FIG. 164



FIG. 165

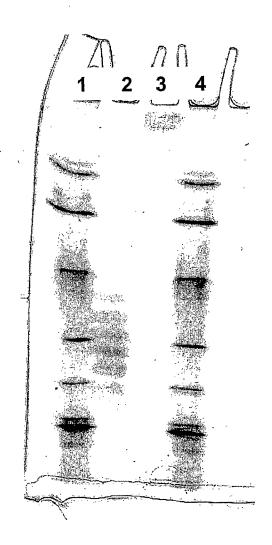


FIG. 166

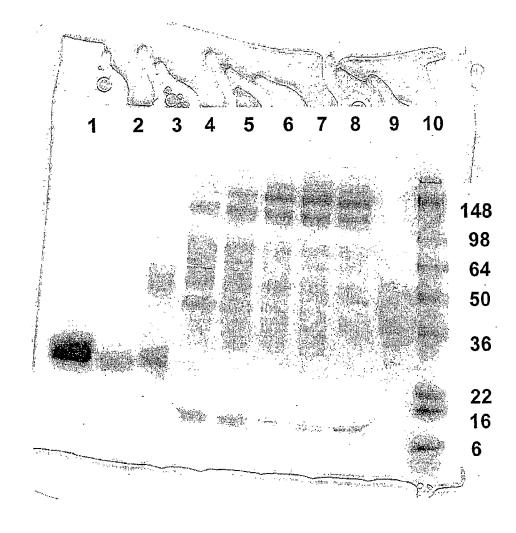


FIG. 167

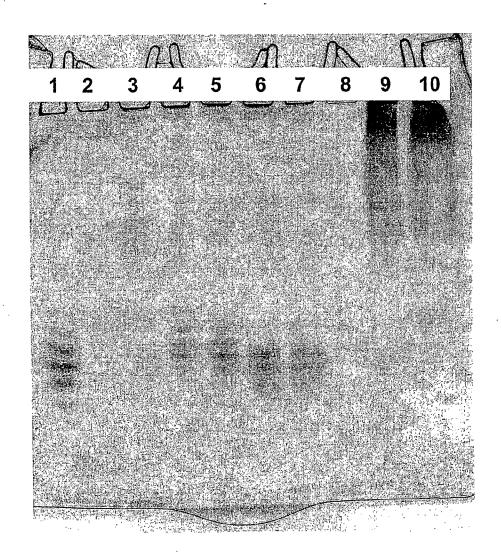
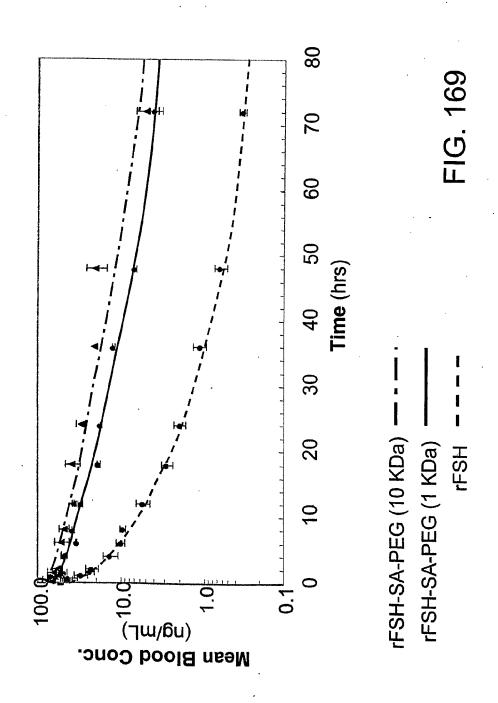


FIG. 168



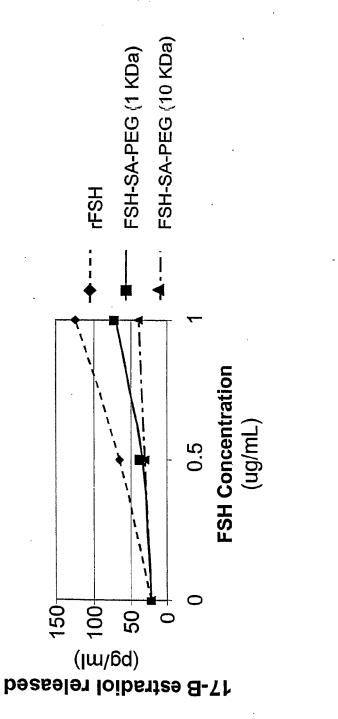
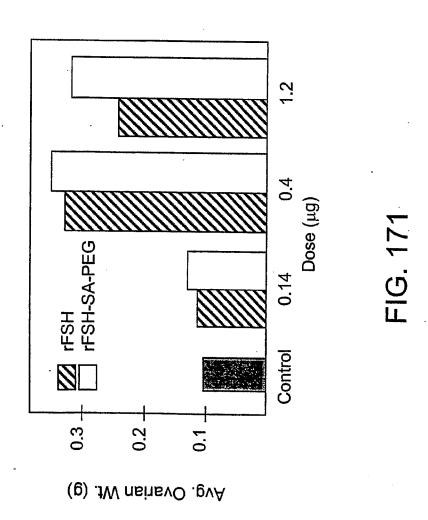
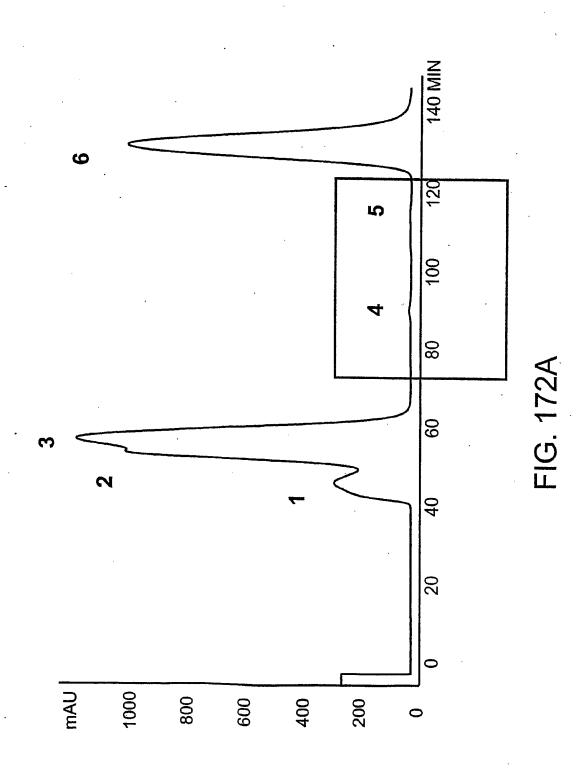
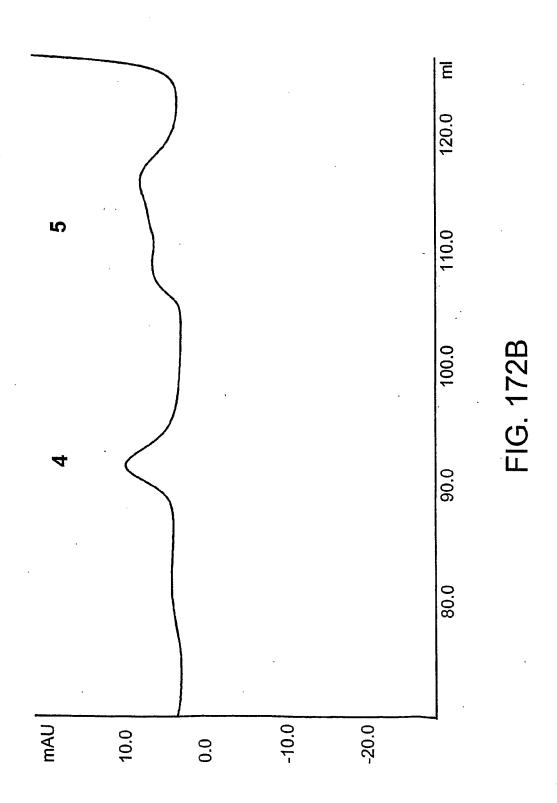
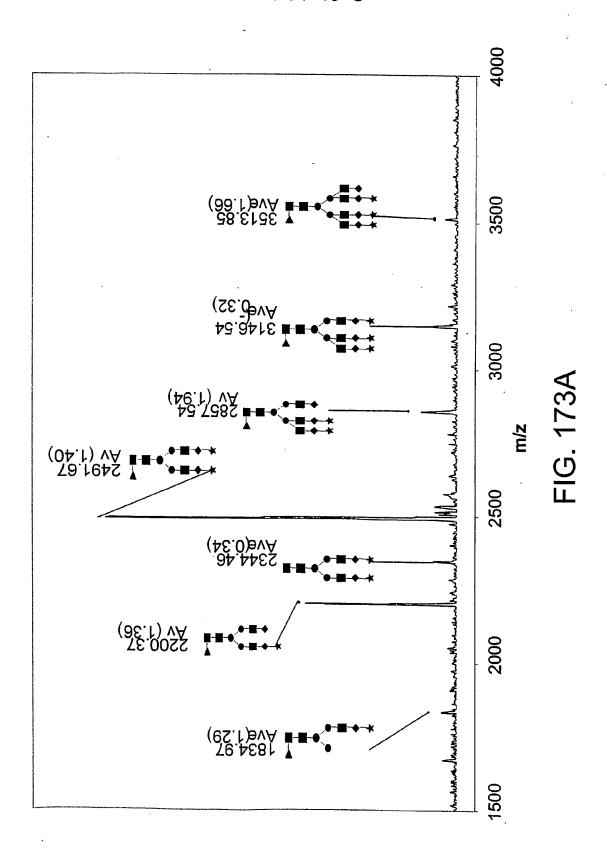


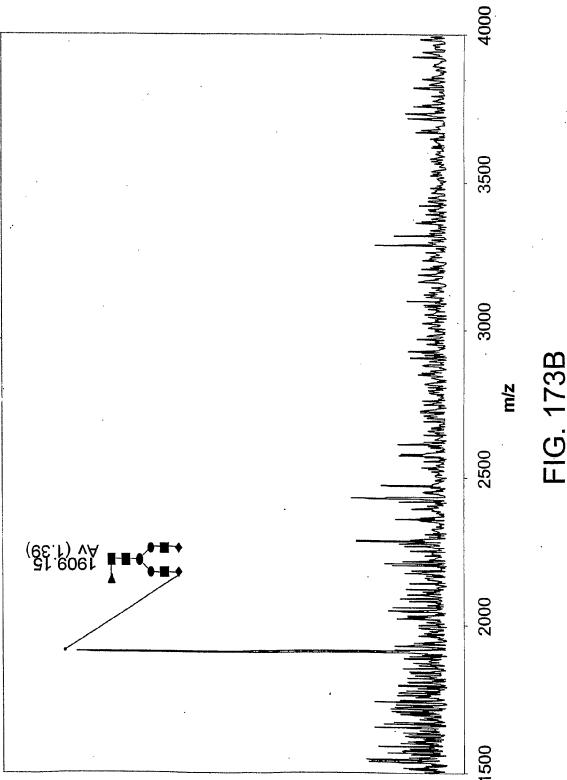
FIG. 170

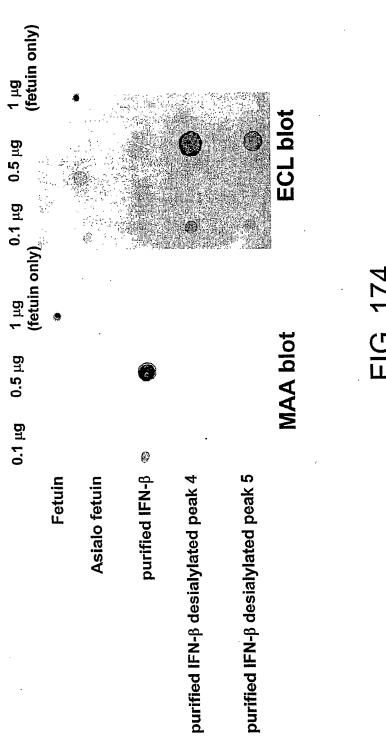












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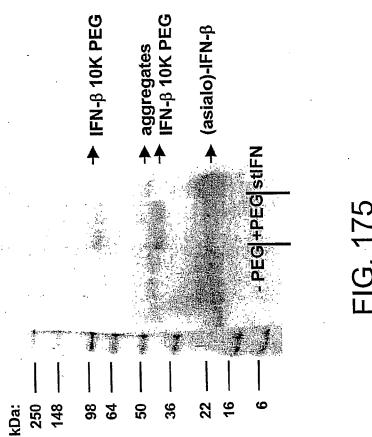
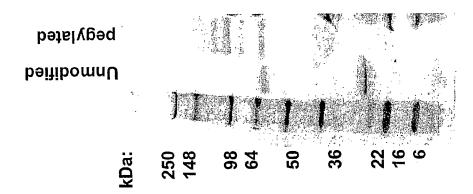
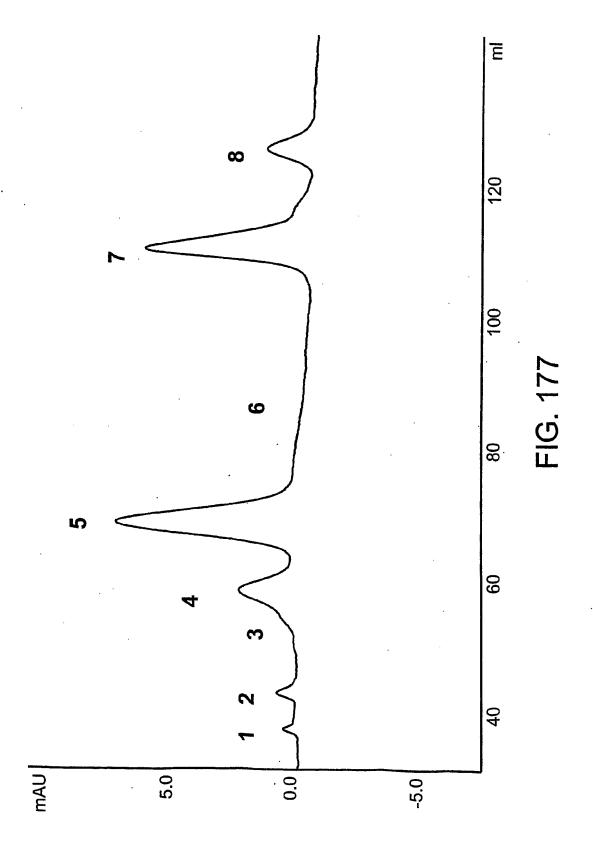
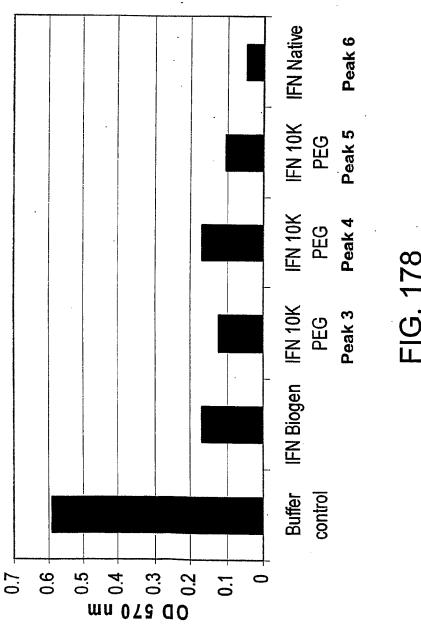


FIG. 176

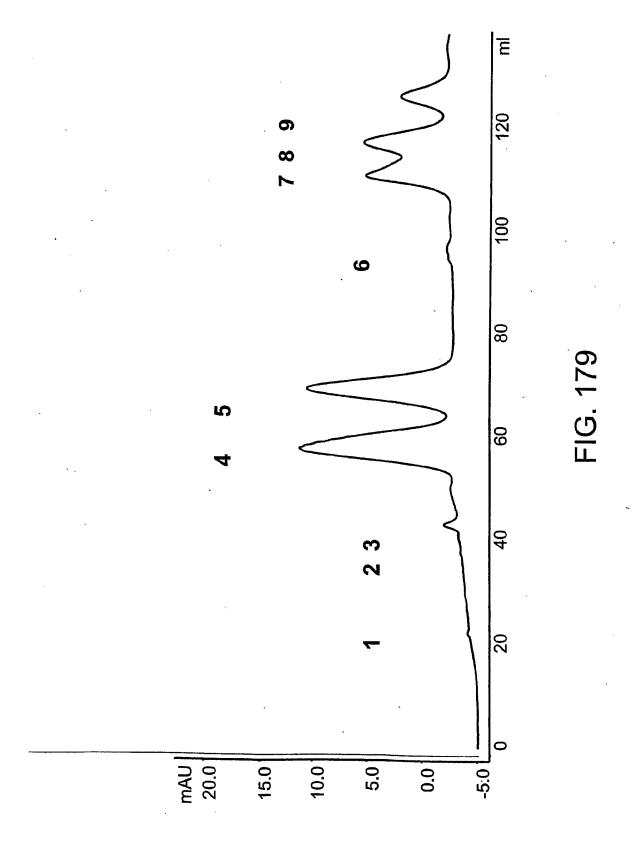


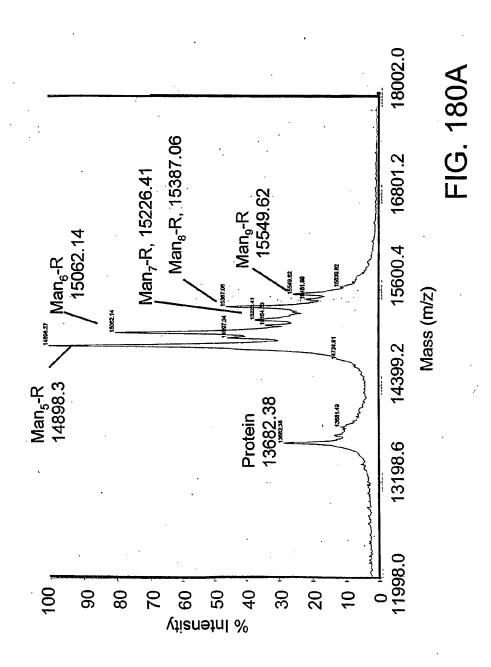
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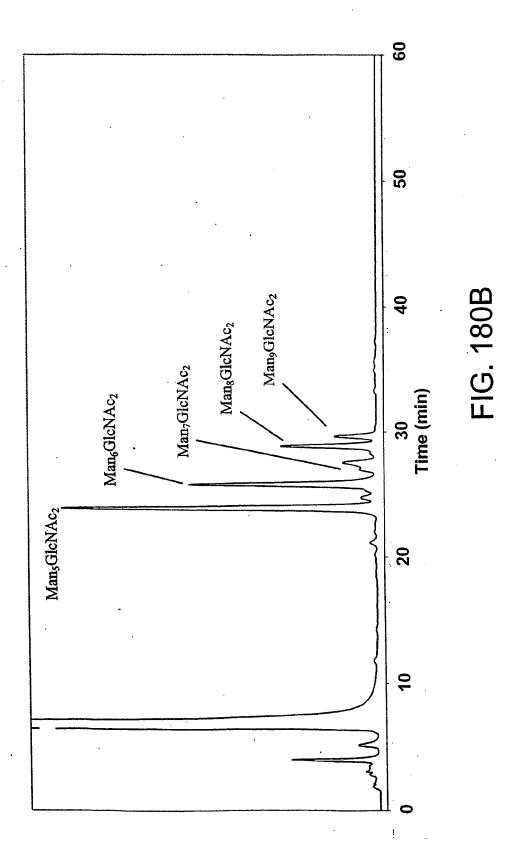




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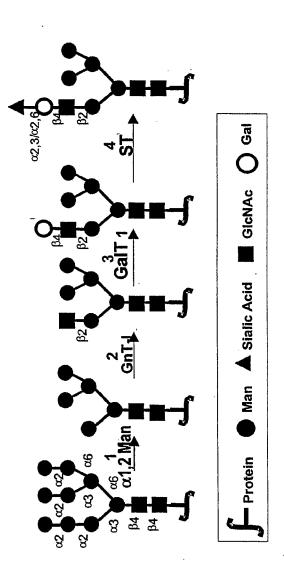


FIG. 181

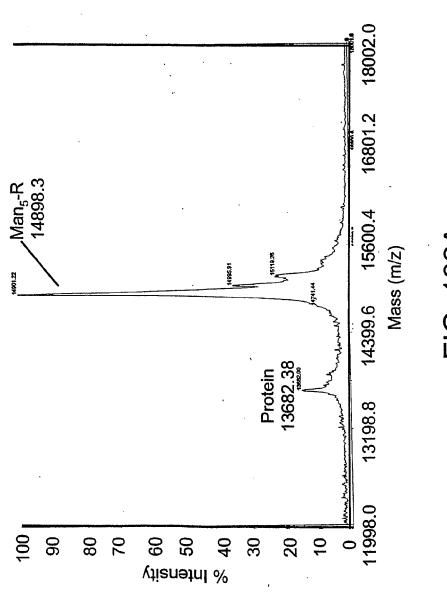
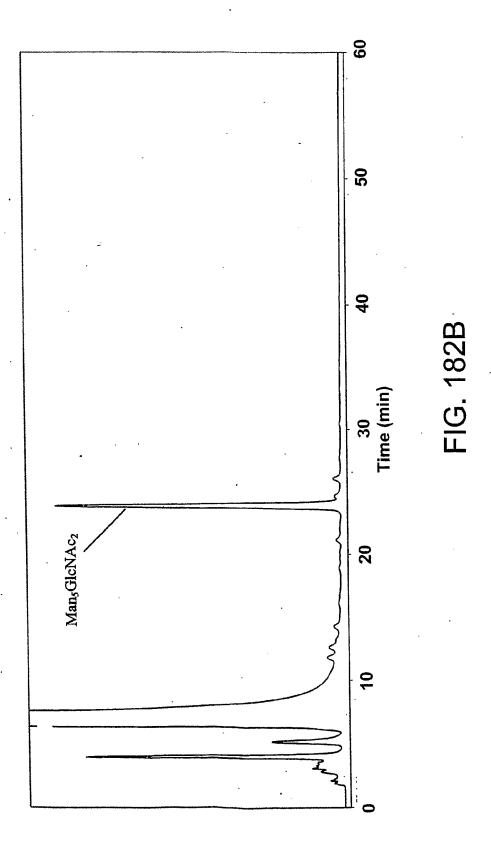
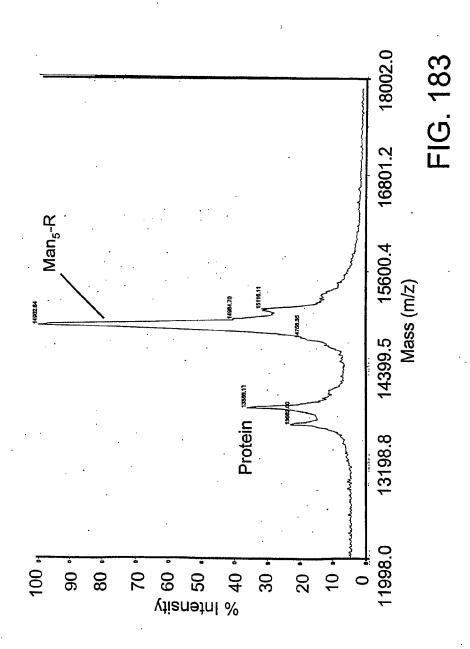
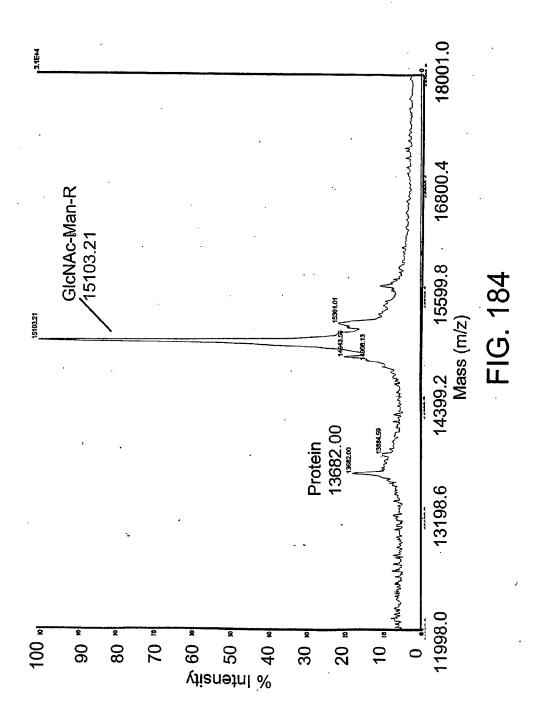
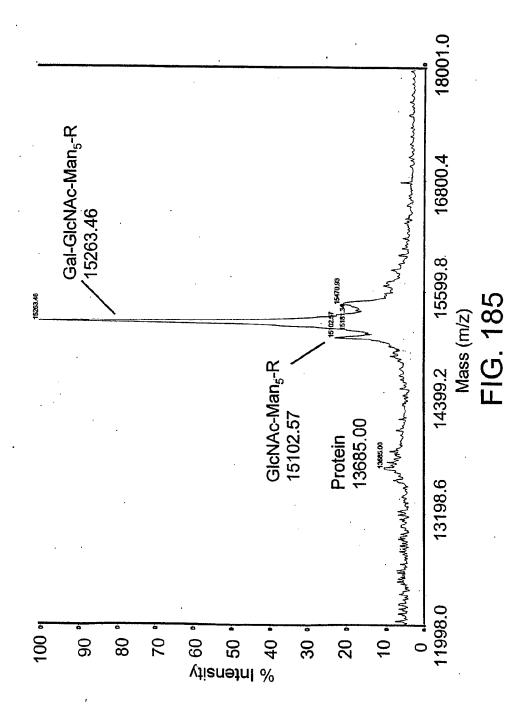


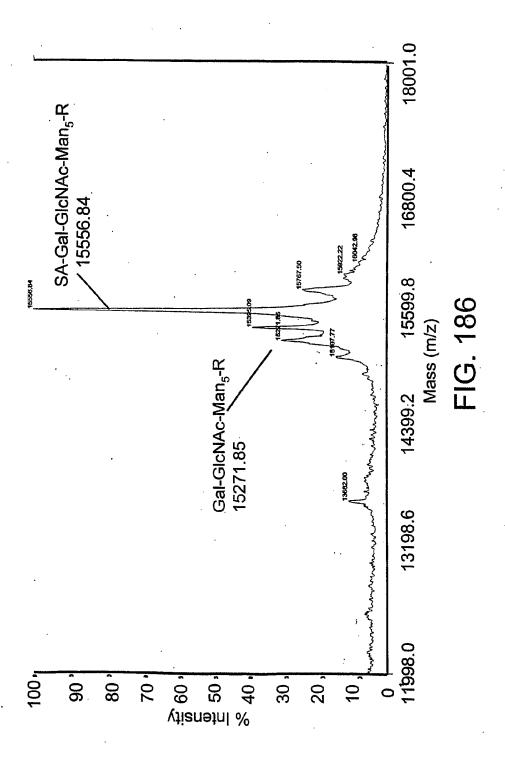
FIG. 182A











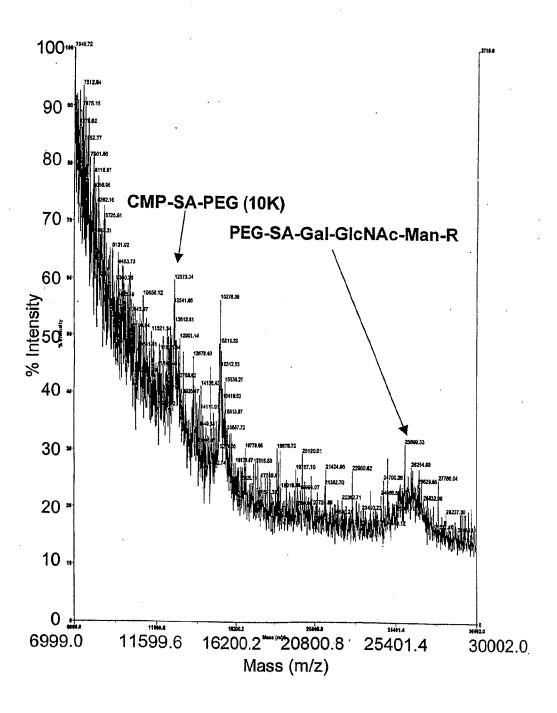


FIG. 187A

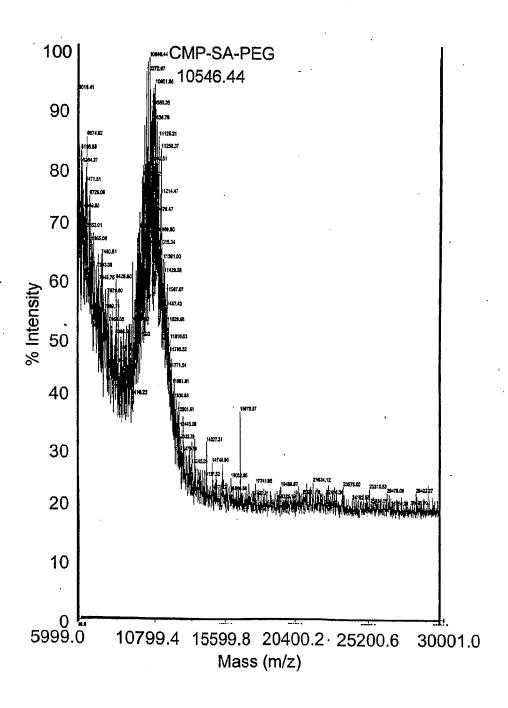
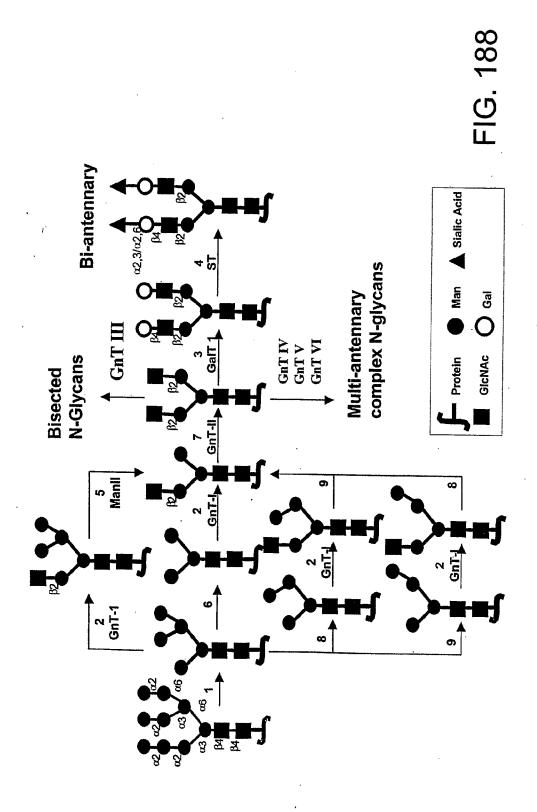


FIG. 187B



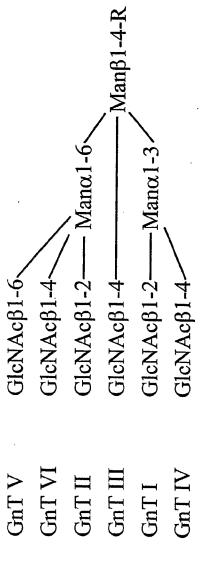


FIG. 189

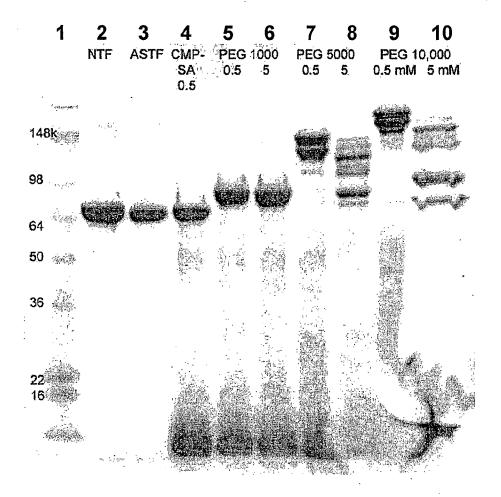


FIG. 190

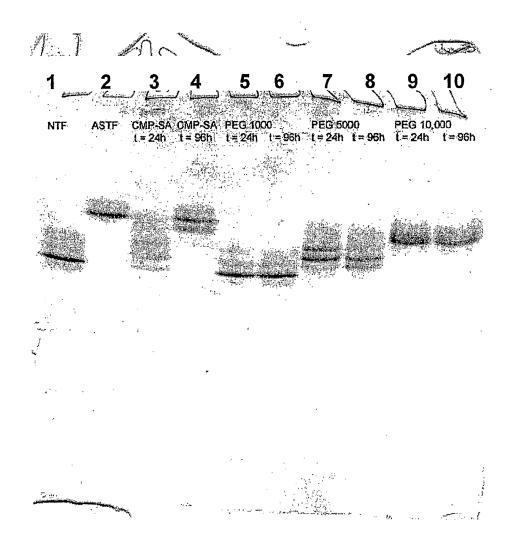
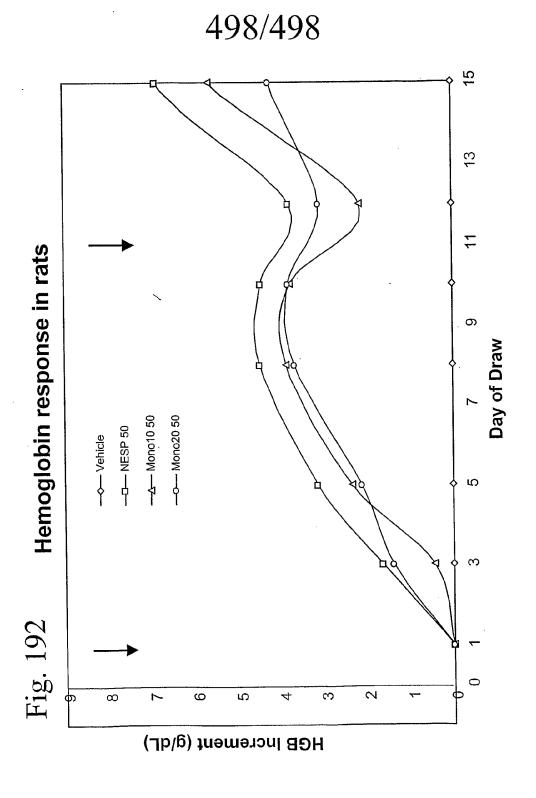


FIG. 191



SEQUENCE LISTING

| <110> | DeFi Zopi Baye Hake Cher | se Technolog rees, Shawn I, David er, Robert es, David n, Xi e, Caryne | gies, | Inc. | | | | | | | | | |
|---------------------------|---|--|--------|--------|------------|------------|------------|-----|--|--|--|--|--|
| <120> | ERYTHROPOIETIN: REMODELING AND GLYCOCONJUGATION OF ERYTHROPOIETIN | | | | | | | | | | | | |
| <130> | 040853-01-5083WO | | | | | | | | | | | | |
| <150> <151> | PCT/US02/32263 2002-10-09 | | | | | | | | | | | | |
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Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val 35 40 45

Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys 50 55 60

Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser 65 70 75 80

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 85 90 95

Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 100 105 110

Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro 115 120 125

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 130 135 140

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| Gly Ser Arg 35 | Arg Thr L | eu Met Leu 40 | Leu Ala Gl | n Met Arg Aro 45 | g Ile Ser | |
| Leu Phe Ser 50 | Cys Leu L | ys Asp Arg 55 | His Asp Ph | e Gly Phe Pro | o Gln Glu | |
| Glu Phe Gly 65 | | he Gln Lys O | Ala Glu Th 75 | r Ile Pro Va | l Leu His 80 | |

3

Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser

| V | / O 2 0 | 04/03 | 3651 | | | | | | | | | | | P | CT/US2 | 003/0319 |
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| Ala | Ala | Trp | Asp 100 | Glu | Thr | Leu | Leu | Asp 105 | Lys | Phe | Tyr | Thr | Glu 110 | Leu | Tyr | |
| Gln | Gln | Leu 115 | Asn | Asp | Leu | Glu | Ala 120 | Cys | Val | Ile | Gln | Gly 125 | Val | Gly | Val | |
| Thr | Glu 130 | Thr | Pro | Leu | Met | Lys 135 | Glu | Asp | Ser | Ile | Leu 140 | Ala | Val | Arg | Lys | |
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| Cys | Ala | Trp | Glu | Val 165 | Val | Arg | Ala | Glu | Ile 170 | Met | Arg | Ser | Phe | Ser 175 | Leu | |
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1080

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6

170

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile

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| Val | Leu | Asn | Val 340 | Pro | Arg | Leu | Met | Thr 345 | Gln | Asp | Cys | Leu | Gln 350 | Gln | Ser | |
| Arg | Lys | Val 355 | Gly | Asp | Ser | Pro | Asn 360 | Ile | Thr | Glu | Tyr | Met 365 | Phe | Cys | Ala | |
| Gly | Tyr 370 | Ser | Asp | Gly | Ser | Lys 375 | Asp | Ser | Cys | Lys | Gly 380 | Asp | Ser | Gly | Gly | |
| Pro 385 | His | Ala | Thr | His | Tyr 390 | Arg | Gly | Thr | Trp | Tyr 395 | Leu | Thr | Gly | Ile | Val 400 | |
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Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn 35 40 45

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Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn 75

Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile 105

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe 135

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Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala 180

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Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile 245

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly 265

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His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His 295

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Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly

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Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu 375 380

Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His 405 410 Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val 440 Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr 450 455 <210> 11 <211> 603 <212> DNA <213> Homo sapiens <400> 11 atggattact acagaaaata tgcagctatc tttctggtca cattgtcggt gtttctgcat 60 gttctccatt ccgctcctga tgtgcaggat tgcccagaat gcacgctaca ggaaaaccca 120 ttottotoco agoogggtgo cocaatactt cagtgoatgg gotgotgott ototagagoa 180 tateceaete eactaaqqte caaqaaqaeq atgttggtee aaaagaaegt caeeteagag 240 tccacttgct gtgtagctaa atcatataac agggtcacag taatgggggg tttcaaagtg 300 qaqaaccaca cggcgtgcca ctgcagtact tgttattatc acaaatctta aatgttttac 360 caaqtqctqt cttqatqact qctqattttc tggaatggaa aattaagttg tttagtgttt 420 atggetttgt gagataaaac teteetttte ettaceatae eaetttgaca egetteaagg 480 atatactqca qctttactqc cttcctcctt atcctacagt acaatcagca gtctagttct 540 600 tttcatttgg aatgaataca gcattaagct tgttccactg caaataaagc cttttaaatc 603 atc <210> 12 <211> 116 <212> PRT Homo sapiens <213> <400> 12 Met Asp Tyr Tyr Arq Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro 20 25 30 Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro 55

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu 70 Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser 115 <210> 13 <211> 390 <212> DNA <213> Homo sapiens <400> 13 60 atqaaqacac tccaqttttt cttccttttc tgttgctgga aagcaatctg ctgcaatagc tgtgagctga ccaacatcac cattgcaata gagaaagaag aatgtcgttt ctgcataagc 120 180 atcaacacca cttggtgtgc tggctactgc tacaccaggg atctggtgta taaggaccca 240 qccaqqccca aaatccaqaa aacatgtacc ttcaaggaac tggtatatga aacagtgaga 300 gtgcccggct gtgctcacca tgcagattcc ttgtatacat acccagtggc cacccagtgt cactgtggca agtgtgacag cgacagcact gattgtactg tgcgaggcct ggggcccagc 360 390 tactgctcct ttggtgaaat gaaagaataa <210> 14 <211> 129 <212> PRT <213> Homo sapiens <400> 14 Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile 5 10 Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly 45 Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys 105 110 Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys

120 125 115

Glu

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| Met 1 | GТУ | Val | His | GLu 5 | Cys | Pro | Ala | Trp | Leu 10 | Trp | ьeu | Leu | Leu | 15 | Leu | |
| Leu | Ser | Leu | Pro 20 | Leu | Gly | Leu | Pro | Val 25 | Leu | Gly | Ala | Pro | Pro 30 | Arg | Leu | |
| Ile | Суз | Asp 35 | Ser | Arg | Val | Leu | Glu 40 | Arg | Tyr | Leu | Leu | Glu 45 | Ala | Lys | Glu | |
| Ala | Glu 50 | Asn | Ile | Thr | Thr | Gly 55 | Cys | Ala | Glu | His | Cys 60 | Ser | Leu | Asn | Glu | |
| Asn 65 | Ile | Thr | Val | Pro | Asp 70 | Thr | Lys | Val | Asn | Phe 75 | Tyr | Ala | Trp | Lys | Arg 80 | |
| Met | Glu | Val | Gly | Gln 85 | Gln | Ala | Val | Glu | Val 90 | Trp | Gln | Gly | Leu | Ala 95 | Leu | |
| Leu | Ser | Glu | Ala 100 | Val | Leu | Arg | Gly | Gln 105 | Ala | Leu | Leu | Val | Asn 110 | Ser | Ser | |
| Gln | Pro | Trp 115 | Glu | Pro | Leu | Gln | Leu 120 | His | Val | Asp | Lys | Ala 125 | Val | Ser | Gly | |
| Leu | Arg 130 | Ser | Leu | Thr | Thr | Leu 135 | Leu | Arg | Ala | Leu | Arg 140 | Ala | Gln | Lys | Glu | |
| Ala 145 | Ile | Ser | Pro | Pro | Asp 150 | Ala | Ala | Ser | Ala | Ala 155 | Pro | Leu | Arg | Thr | Ile 160 | |
| Thr | Ala | Asp | Thr | Phe 165 | Arg | Lys | Leu | Phe | Arg 170 | Val | Tyr | Ser | Asn | Phe 175 | Leu | |
| Arg | Gly | Lys | Leu 180 | | Leu | Tyr | Thr | Gly 185 | Glu | Ala | Суз | Arg | Thr 190 | Gly | Asp | |
| Arg | | | | | | | | | | | | | | | | |
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| cgc | tcgc | cca | gccc | cago | ac g | cagc | cctg | g ga | gcat | gtga | atg | ccat | cca | ggag | gcccgg | 120 |
| cgt | ctcc | tga | acct | gagt | ag a | gaca | ctgc | t gc | tgag | atga | atg | aaac | agt | agaa | gtcatc | 180 |
| tca | gaaa | tgt | ttga | cctc | ca g | gago | cgac | c tg | ccta | caga | ccc | gcct | gga | gctg | tacaag | 240 |
| cag | ggcc | tgc | agaa | cago | ct c | acca | agct | c aa | gggc | ccct | tga | .ccat | gat | ggcc | agccac | 300 |
| tac | aagc | agc | actg | rccct | .cc a | acco | cgga | a ac | ttcc | tgtg | caa | ccca | .gat | tato | accttt | 360 |
| ~== | actt | tca | aaga | เสลลด | at o | raago | actt | t ct | actt | at.ca | tcc | cctt | tga | ctac | tgggag | 420 |

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<213> Homo sapiens

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Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp 35 40 45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
50 55 60

Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys 65 70 75 80

Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met 85 90 95

Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser

Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys 115 120 125

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Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn 35 40 45

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp 50 55 60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe 65 70 75 80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile 85 90 95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Arg 100 105 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val 115 120 125

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser 130 135 140

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| cgaagaggcc aagaaacaga | tcaacgatta | cgtggagaag | ggtactcaag | ggaaaattgt | 600 |
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| ggatttggtc aaggagcttg | acagagacac | agtttttgct | ctggtgaatt | acatcttctt | 660 |
| taaaggcaaa tgggagagac | cctttgaagt | caaggacacc | gaggaagagg | acttccacgt | 720 |
| ggaccaggtg accaccgtga | aggtgcctat | gatgaagcgt | ttaggcatgt | ttaacatcca | 780 |
| gcactgtaag aagctgtcca | gctgggtgct | gctgatgaaa | tacctgggca | atgccaccgc | 840 |
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| tatcatcacc aagttcctgg | aaaatgaaga | cagaaggtct | gccagcttac | atttacccaa | 960 |
| actgtccatt actggaacct | atgatctgaa | gagcgtcctg | ggtcaactgg | gcatcactaa | 1020 |
| ggtcttcagc aatggggctg | acctctccgg | ggtcacagag | gaggcacccc | tgaagctctc | 1080 |
| caaggeegtg cataaggetg | tgctgaccat | cgacgagaaa | gggactgaag | ctgctggggc | 1140 |
| catgttttta gaggccatac | ccatgtctat | ccccccgag | gtcaagttca | acaaaccctt | 1200 |
| tgtcttctta atgattgaac | aaaataccaa | gtctcccctc | ttcatgggaa | aagtggtgaa | 1260 |
| tcccacccaa aaataactgc | ctctcgctcc | tcaacccctc | ccctccatcc | ctggccccct | 1320 |
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<212> PRT

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Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn 35 40 45

Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln 50 55 60

Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser 65 70 75 80

Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr $85 \\ 90 \\ 95$

His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro 100 105 110

Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Arg Thr Leu Asn 115 120 125

Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu 130 135 140

Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys 185 Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu 200 Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val 215 Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys 250 Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala 260 Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu 280 Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr 310 Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe 325 Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys 345 Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly 360 355 Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile 375 Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu 390 395 Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr 405 410 Gln Lys <210> 23 <211> 2004 <212> DNA <213> Homo sapiens <400> 23 qctaacctag tgcctatagc taaggcaggt acctgcatcc ttgtttttgt ttagtggatc 60

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| tcatggctgg | cagcctcaca | ggtttgcttc | tacttcaggc | agtgtcgtgg | gcatcaggtg | 240 |
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| catactgtga | ctcctttgac | cccccgacct | ttcctgccct | tggtaccttc | agccgctatg | 360 |
| agagtacacg | cagtgggcga | cggatggagc | tgagtatggg | gcccatccag | gctaatcaca | 420 |
| cgggcacagg | cctgctactg | accctgcagc | cagaacagaa | gttccagaaa | gtgaagggat | 480 |
| ttggaggggc | catgacagat | gctgctgctc | tcaacatcct | tgccctgtca | cccctgccc | 540 |
| aaaatttgct | acttaaatcg | tacttctctg | aagaaggaat | cggatataac | atcatccggg | 600 |
| tacccatggc | cagctgtgac | ttctccatcc | gcacctacac | ctatgcagac | acccctgatg | 660 |
| atttccagtt | gcacaacttc | agcctcccag | aggaagatac | caagctcaag | atacccctga | 720 |
| ttcaccgagc | cctgcagttg | gcccagcgtc | ccgtttcact | ccttgccagc | ccctggacat | 780 |
| cacccacttg | gctcaagacc | aatggagcgg | tgaatgggaa | ggggtcactc | aagggacagc | 840 |
| ccggagacat | ctaccaccag | acctgggcca | gatactttgt | gaagttcctg | gatgcctatg | 900 |
| ctgagcacaa | gttacagttc | tgggcagtga | cagctgaaaa | tgagccttct | gctgggctgt | 960 |
| tgagtggata | ccccttccag | tgcctgggct | tcacccctga | acatcagcga | gacttcattg | 1020 |
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| taaaccgctc | ctctaaggat | gtgcctctta | ccatcaagga | tcctgctgtg | ggcttcctgg | 1680 |
| agacaatctc | acctggctac | tccattcaca | cctacctgtg | gcatcgccag | tgatggagca | 1740 |
| gatactcaag | gaggcactgg | gctcagcctg | ggcattaaag | ggacagagtc | agctcacacg | 1800 |
| ctgtctgtga | ctaaagaggg | cacagcaggg | ccagtgtgag | cttacagcga | cgtaagccca | 1860 |
| ggggcaatgg | tttgggtgac | tcactttccc | ctctaggtgg | tgcccagggc | tggaggcccc | 1920 |

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Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu 65 70 75 80

Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln 85 90 95

Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln
100 105 110

Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala 115 120 125

Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu 130 135 140

Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val 145 150 155 160

Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp 165 170 175

Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp 180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln 195 200 205

Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu 210 215 220

Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro 225 230 235 240

Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu 245 250 255

Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu 260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly 295 Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Pro His Trp Ala Lys Val Val Leu Thr 325 330 Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg 360 Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp 425 Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp 435 Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys 455 Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys 465 470 Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val 490 485 Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys 500 505 Asp Pro Ala Val Gly Phe Leu Glu Thr .Ile Ser Pro Gly Tyr Ser Ile 525 520 His Thr Tyr Leu Trp His Arg Gln 530 535 <210> 25 <211> 1726 <212> DNA <213> Homo sapiens atggatgcaa tgaaqaqagg gctctgctgt gtgctgctgc tgtgtggagc agtcttcgtt tegeccagee aggaaateea tgeecgatte agaagaggag ccagatetta ecaagtgate

| tgcagagatg | aaaaaacgca | gatgatatac | cagcaacatc | agtcatggct | gcgccctgtg | 180 |
|------------|------------|------------|------------|------------|------------|------|
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| gtgcctgtca | aaagttgcag | cgagccaagg | tgtttcaacg | ggggcacctg | ccagcaggcc | 300 |
| ctgtacttct | cagatttcgt | gtgccagtgc | cccgaaggat | ttgctgggaa | gtgctgtgaa | 360 |
| atagatacca | gggccacgtg | ctacgaggac | cagggcatca | gctacagggg | cacgtggagc | 420 |
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| ctgcatttct | ttggtggggg | gccaggaggg | tgcatccaat | ttaacttaac | tcttacctat | 7260 |
| tttctgcagc | tgctcccaga | ttactccttc | cttccaatat | aactaggcaa | aaagaagtga | 7320 |

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Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg 35 40 45

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val 50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile 65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
85 90 95

Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser 100 105 110

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser 115 120 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp 130 135 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu 145 150 155 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser 165 170 175

| Tyr | Leu | Ser | His 180 | Val | Asp | Leu | Val | Lys 185 | Asp | Leu | Asn | Ser | G1y 190 | Leu | Ile |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Gly | Ala | Leu 195 | Leu | Val | Cys | Arg | Glu 200 | Gly | Ser | Leu | Ala | Lys 205 | Glu | Lys | Thr |
| Gln | Thr 210 | Leu | His | Lys | Phe | Ile 215 | Leu | Leu | Phe | Ala | Val 220 | Phe | Asp | Glu | Gly |
| Lys 225 | Ser | Trp | His | Ser | Glu 230 | Thr | Lys | Asn | Ser | Leu 235 | Met | Gln | Asp | Arg | Asp 240 |
| Ala | Ala | Ser | Ala | Arg 245 | Ala | Trp | Pro | Lys | Met 250 | His | Thr | Val | Asn | Gly 255 | Tyr |
| Val | Asn | Arg | Ser 260 | Leu | Pro | Gly | Leu | Ile 265 | Gly | Cys | His | Arg | Lys 270 | Ser | Val |
| Tyr | Trp | His 275 | Val | Ile | Gly | Met | Gly 280 | Thr | Thr | Pro | Glu | Val 285 | His | Ser | Ile |
| Phe | Leu 290 | Glu | Gly | His | Thr | Phe 295 | Leu | Val | Arg | Asn | His 300 | Arg | Gln | Ala | Ser |
| Leu 305 | Glu | Ile | Ser | Pro | Ile 310 | Thr | Phe | Leu | Thr | Ala 315 | Gln | Thr | Leu | Leu | Met 320 |
| Asp | Leu | Gly | Gln | Phe 325 | Leu | Leu | Phe | Суз | His 330 | Ile | Ser | Ser | His | Gln 335 | His |
| Asp | Gly | Met | Glu 340 | Ala | Tyr | Val | Lys | Val 345 | Asp | Ser | Cys | Pro | Glu 350 | Glu | Pro |
| Gln | Leu | Arg 355 | Met | Lys | Asn | Asn | Glu 360 | Glu | Ala | Glu | Asp | Tyr 365 | Asp | Asp | Asp |
| Leu | Thr 370 | Asp | Ser | Glu | Met | Asp 375 | Val | Val | Arg | Phe | Asp 380 | Asp | Asp | Asn | Ser |
| Pro 385 | Ser | Phe | Ile | Gln | Ile 390 | Arg | Ser | Val | Ala | Lys 395 | Lys | His | Pro | Lys | Thr 400 |
| Trp | Val | His | Tyr | Ile 405 | Ala | Ala | Glu | Glu | Glu 410 | Asp | Trp | Asp | Tyr | Ala 415 | Pro |
| Leu | Val | Leu | Ala 420 | | Asp | Asp | Arg | Ser 425 | Tyr | Lys | Ser | Gln | Tyr 430 | Leu | Asn |
| Asn | Gly | Pro 435 | Gln | Arg | Ile | Gly | Arg 440 | Lys | Tyr | Lys | Lys | Val 445 | Arg | Phe | Met |
| Ala | Tyr 450 | Thr | Asp | Glu | Thr | Phe 455 | Lys | Thr | Arg | Glu | Ala 460 | Ile | Gln | His | Glu |
| Ser 465 | Gly | Ile | Leu | Gly | Pro 470 | Leu | Leu | Tyr | Gly | Glu 475 | Val | Gly | Asp | Thr | Leu 480 |
| Leu | Ile | Ile | Phe | Lys 485 | Asn | Gln | Ala | Ser | Arg 490 | Pro | Tyr | Asn | Ile | Tyr 495 | Pro |
| His | Gly | Ile | Thr | Asp | Val | Arg | Pro | Leu | Tyr | Ser | Arg | Arg | Leu | Pro | Lys |

500 505 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 520 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg 550 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 585 Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 600 Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 615 Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 650 Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg 760 Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp 775 Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys 790 795

Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser 805 810 815

Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr

Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys 885 890 Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn 905 Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met 920 Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys 935 Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu 965 970 Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser 1015 Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser 1025 1030 Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu 1045 Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg 1055 1060 1065 Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met 1075 Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln 1085 1090 1.095 Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met 1100 1105 1110 Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile 1115 1120 1125 Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro 1130 1135 1140

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| Gly | Glu 1175 | Phe | Thr | Lys | Asp | Val 1180 | Gly | Leu | Lys | Glu | Met 1185 | Val | Phe | Pro |
| Ser | Ser 1190 | Arg | Asn | Leu | Phe | Leu 1195 | Thr | Asn | Leu | Asp | Asn 1200 | Leu | His | Glu |
| Asn | Asn 1205 | Thr | His | Asn | Gln | Glu 1210 | Lys | Lys | Ile | Gln | Glu 1215 | Glu | Ile | Glu |
| Lys | Lys 1220 | Glu | Thr | Leu | Ile | Gln 1225 | Glu | Asn | Val | Val | Leu 1230 | Pro | Gln | Ile |
| His | Thr 1235 | Val | Thr | Gly | Thr | Lys 1240 | | Phe | Met | Lys | Asn 1245 | Leu | Phe | Leu |
| Leu | Ser 1250 | Thr | Arg | Gln | Asn | Val 1255 | Glu | Gly | Ser | Tyr | Asp 1260 | Gly | Ala | Tyr |
| Ala | Pro 1265 | Val | Leu | Gln | Asp | Phe 1270 | Arg | Ser | Leu | Asn | Asp 1275 | Ser | Thr | Asn |
| Arg | Thr 1280 | | Lys | His | Thr | Ala 1285 | His | Phe | Ser | Lys | Lys 1290 | Gly | Glu | Glu |
| Glu | Asn 1295 | Leu | Glu | Gly | Leu | Gly 1300 | Asn | Gln | Thr | Lys | Gln 1305 | Ile | Val | Glu |
| Lys | Tyr 1310 | | Cys | Thr | Thr | Arg 1315 | Ile | Ser | Pro | Asn | Thr 1320 | Ser | Gln | Gln |
| Asn | Phe 1325 | | Thr | Gln | Arg | Ser 1330 | | Arg | Ala | Leu | Lys 1335 | Gln | Phe | Arg |
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| Asp | Thr 1355 | | Thr | Gln | Trp | Ser 1360 | Lys | Asn | Met | Lys | His 1365 | Leu | Thr | Pro |
| Ser | Thr 1370 | | Thr | Gln | Ile | Asp 1375 | | Asn | Glu | Lys | Glu 1380 | | Gly | Ala |
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| Ile | Pro 1400 | | Ala | Asn | Arg | Ser 1405 | | Leu | Pro | Ile | Ala 1410 | Lys | Val | Ser |
| Ser | Phe 1415 | | Ser | Ile | Arg | Pro 1420 | | Tyr | Leu | Thr | Arg 1425 | Val | Leu | Phe |
| Gln | Asp 1430 | | Ser | Ser | His | Leu 1435 | | Ala | Ala | Ser | Tyr 1440 | | Lys | Lys |
| Asp | Ser | Gly | Val | Gln | Glu | Ser | Ser | His | Phe | Leu | Gln | Gly | Ala | Lys |

| , | VO 200 | 14/033 | 651 | | | | | | | | | | | PC17U |
|-----|---------------|--------|-----|-----|-----|-------------|-----|-----|-----|-----|-------------|-----|-----|-------|
| | 1445 | | | | | 1450 | | | | | 1455 | | | |
| Lys | Asn 1460 | Asn | Leu | Ser | Leu | Ala 1465 | Ile | Leu | Thr | Leu | Glu 1470 | Met | Thr | Gly |
| Asp | Gln 1475 | Arg | Glu | Val | Gly | Ser 1480 | Leu | Gly | Thr | Ser | Ala 1485 | Thr | Asn | Ser |
| Val | Thr 1490 | Tyr | Lys | Lys | Val | Glu 1495 | Asn | Thr | Val | Leu | Pro 1500 | | Pro | Asp |
| Leu | Pro 1505 | Lys | Thr | Ser | Gly | Lys 1510 | Val | Glu | Leu | Leu | Pro 1515 | Lys | Val | His |
| Ile | Tyr 1520 | | Lys | Asp | | Phe 1525 | Pro | Thr | Glu | Thr | Ser 1530 | Asn | Gly | Ser |
| Pro | Gly 1535 | His | Leu | Asp | Leu | Val 1540 | | Gly | Ser | Leu | Leu 1545 | Gln | Gly | Thr |
| Glu | Gly 1550 | Ala | Ile | Lys | Trp | Asn 1555 | Glu | Ala | Asn | Arg | Pro 1560 | Gly | Lys | Val |
| Pro | Phe 1565 | Leu | Arg | Val | | Thr 1570 | Glu | Ser | Ser | Ala | Lys 1575 | Thr | Pro | Ser |
| Lys | Leu 1580 | Leu | Asp | Pro | Leu | Ala 1585 | | Asp | Asn | His | Tyr 1590 | Gly | Thr | Gln |
| Ile | Pro 1595 | Lys | Glu | Glu | Trp | Lys 1600 | Ser | Gln | Glu | Lys | Ser 1605 | Pro | Glu | Lys |
| Thr | Ala 1610 | Phe | Lys | Lys | Lys | Asp 1615 | Thr | Ile | Leu | | Leu 1620 | Asn | Ala | Cys |
| Glu | Ser 1625 | | His | Ala | Ile | Ala 1630 | | Ile | Asn | Glu | Gly 1635 | | Asn | Lys |
| Pro | Glu 1640 | Ile | Glu | Val | Thr | Trp 1645 | Ala | Lys | Gln | Gly | Arg 1650 | Thr | Glu | Arg |
| Leu | Cys 1655 | | Gln | Asn | Pro | Pro 1660 | Val | Leu | Lys | Arg | His 1665 | Gln | Arg | Glu |
| Ile | Thr 1670 | _ | Thr | Thr | Leu | Gln 1675 | Ser | Asp | Gln | Glu | Glu 1680 | | Asp | Tyr |
| Asp | Asp 1685 | | Ile | Ser | Val | Glu 1690 | | Lys | Lys | Glu | Asp 1695 | | Asp | Ile |
| Tyr | Asp 1700 | | Asp | Glu | Asn | Gln 1705 | Ser | Pro | Arg | Ser | Phe 1710 | | Lys | Lys |
| Thr | Arg 1715 | | Tyr | Phe | Ile | Ala 1720 | | Val | Glu | Arg | Leu 1725 | | Asp | Tyr |
| Gly | Met 1730 | | Ser | Ser | Pro | His 1735 | | Leu | Arg | Asn | Arg 1740 | | Gln | Ser |
| Gly | Ser 1745 | | Pro | Gln | Phe | Lys 1750 | | Val | Val | Phe | Gln 1755 | | Phe | Thr |

| Asp | Gly 1760 | Ser | Phe | Thr | Gln | Pro 1765 | Leu | Tyr | Arg | Gly | Glu 1770 | Leu | Asn | Glu |
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| His | Leu 1775 | Gly | Leu | Leu | Gly | Pro 1780 | Tyr | Ile | Arg | Ala | Glu 1785 | Val | Glu | Asp |
| Asn | Ile 1790 | Met | Val | Thr | Phe | Arg 1795 | Asn | Gln | Ala | Ser | Arg 1800 | Pro | Tyr | Ser |
| Phe | Tyr 1805 | Ser | Ser | Leu | Ile | Ser 1810 | Tyr | Glu | Glu | Asp | Gln 1815 | Arg | Gln | Gly |
| Ala | Glu 1820 | Pro | Arg | Lys | Asn | Phe 1825 | Val | Lys | Pro | Asn | Glu 1830 | Thr | Lys | Thr |
| Tyr | Phe 1835 | Trp | Lys | Val | Gln | His 1840 | His | Met | Ala | Pro | Thr 1845 | Lys | Asp | Glu |
| Phe | Asp 1850 | Cys | Lys | Ala | Trp | Ala 1855 | Tyr | Phe | Ser | Asp | Val 1860 | Asp | Leu | Glu |
| Lys | Asp 1865 | | His | Ser | Gly | Leu 1870 | | Gly | Pro | Leu | Leu 1875 | Val | Cys | His |
| Thr | Asn 1880 | Thr | Leu | Asn | Pro | Ala 1885 | | Gly | Arg | Gln | Val 1890 | Thr | Val | Gln |
| | Phe 1895 | | Leu | Phe | Phe | Thr 1900 | | Phe | Asp | Glu | Thr 1905 | Lys | Ser | Trp |
| Tyr | Phe 1910 | | Glu | Asn | Met | Glu 1915 | | Asn | Cys | Arg | Ala 1920 | Pro | Cys | Asn |
| Ile | Gln 1925 | | Glu | Asp | Pro | Thr 1930 | | Lys | Glu | Asn | Tyr 1935 | | Phe | His |
| Ala | Ile 1940 | | Gly | Tyr | Ile | Met 1945 | | Thr | Leu | Pro | Gly 1950 | | Val | Met |
| Ala | Gln 1955 | | Gln | Arg | Ile | Arg 1960 | | Tyr | Leu | Leu | Ser 1965 | | Gly | Ser |
| Asn | Glu 1970 | | Ile | His | Ser | Ile 1975 | | Phe | rSer | Gly | His 1980 | | Phe | Thr |
| Val | Arg 1985 | _ | Lys | Glu | Glu | Tyr 1990 | | Met | Ala | Leu | Tyr 1995 | | Leu | Tyr |
| Pro | Gly 2000 | | Phe | Glu | Thr | Val 2005 | | Met | Leu | Pro | Ser 2010 | | Ala | Gly |
| Ile | Trp 2015 | | Val | Glu | Cys | Leu 2020 | | Gly | Glu | His | Leu 2025 | | Ala | Gly |
| Met | Ser 2030 | | Leu | Phe | Leu | Val 2035 | | Ser | Asn | Lys | Cys 2040 | | Thr | Pro |
| Leu | Gly 2045 | | Ala | Ser | Gly | His 2050 | | Arg | Asp | Phe | Gln 2055 | | Thr | Ala |

| Ser | Gly 2060 | Gln | Tyr | Gly | Gln | Trp 2065 | Ala | Pro | Lys | Leu | Ala 2070 | Arg | Leu | His |
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| Tyr | Ser 2075 | Gly | Ser | Ile | Asn | Ala 2080 | Trp | Ser | Thr | Lys | Glu 2085 | Pro | Phe | Ser |
| Trp | Ile 2090 | Lys | Val | Asp | Leu | Leu 2095 | Ala | Pro | Met | Ile | Ile 2100 | His | Gly | Ile |
| Lys | Thr 2105 | Gln | Gly | Ala | Arg | Gln 2110 | _ | Phe | Ser | Ser | Leu 2115 | Tyr | Ile | Ser |
| Gln | Phe 2120 | Ile | Ile | Met | Tyr | Ser 2125 | Leu | Asp | Gly | Lys | Lys 2130 | Trp | Gln | Thr |
| Tyr | Arg 2135 | | Asn | Ser | Thr | Gly 2140 | Thr | Leu | Met | Val | Phe 2145 | Phe | Gly | Asn |
| Val | Asp 2150 | | Ser | Gly | Ile | Lys 2155 | His | Asn | Ile | Phe | Asn 2160 | Pro | Pro | Ile |
| Ile | Ala 2165 | - | Tyr | Ile | Arg | Leu 2170 | His | Pro | Thr | His | Tyr 2175 | Ser | Ile | Arg |
| Ser | Thr 2180 | Leu | Arg | Met | Glu | Leu 2185 | Met | Gly | Cys | Asp | Leu 2190 | Asn | Ser | Cys |
| Ser | Met 2195 | | Leu | | | Glu 2200 | | Lys | Ala | Ile | Ser 2205 | Asp | Ala | Gln |
| Ile | Thr 2210 | Ala | Ser | Ser | Tyr | Phe 2215 | | Asn | Met | Phe | Ala 2220 | Thr | Trp | Ser |
| Pro | Ser 2225 | | Ala | Arg | Leu | His 2230 | Leu | Gln | Gly | Arg | Ser 2235 | Asn | Ala | Trp |
| Arg | Pro 2240 | | Val | Asn | Asn | Pro 2245 | | Glu | Trp | Leu | Gln 2250 | Val | Asp | Phe |
| Gln | Lys 2255 | | Met | Lys | Val | Thr 2260 | | Val | Thr | Thr | Gln 2265 | | Val | Lys |
| Ser | Leu 2270 | | Thr | Ser | Met | Tyr 2275 | | Lys | Glu | Phe | Leu 2280 | | Ser | Ser |
| Ser | Gln 2285 | | Gly | His | Gln | Trp 2290 | | Leu | Phe | Phe | Gln 2295 | Asn | Gly | Lys |
| Val | Lys 2300 | | Phe | Gln | Gly | Asn 2305 | | Asp | Ser | Phe | Thr 2310 | | Val | Val |
| Asn | Ser 2315 | | Asp | Pro | Pro | Leu 2320 | | Thr | Arg | Tyr | Leu 2325 | | Ile | His |
| Pro | Gln 2330 | | Trp | Val | His | Gln 2335 | | Ala | Leu | Arg | Met 2340 | | Val | Leu |
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325 330 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly 340 345

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser 355 360 365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile 370 375 380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln 385 390 395 400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro 405 410 415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser 420 425 430

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445 \hspace{1.5cm}$

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<400> 33

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<212> PRT

<213> Homo sapiens

<400> 34

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Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp 20 25 30

Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile 50 60

Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly 65 70 75 80

Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser 85 90 95

Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu 100 105 110

Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg 115 120 125

Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
130 135 140

Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro 145 150 155 160

Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg 165 170 175

Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp

180 185 190

Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val 195 200 205

Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His 210 215 220

Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly 225 230 235 240

Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val . 245 250 255

Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His 260 265 270

His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys 275 280 285

Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr 290 295 300

Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys 305 310 315 320

Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val 325 330 335

Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly 340 345 350

Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys 355 360 365

Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu 370 380

Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys 385 390 395 400

Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu 405 410 415

Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu 420 425 430

<210> 35

<211> 107

<212> PRT

<213> Mus musculus

<400> 35

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala 20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Ile $35 \hspace{1cm} 40 \hspace{1cm} 45$

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 36

<211> 120

<212> PRT

<213> Mus musculus

<400> 36

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1 $$ 5 $$ 10 $$ 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val 50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 37

<211> 120

<212> PRT

<213> Mus musculus

<400> 37

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser 20 25 30

Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu 35 40

Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala 100 105 Gly Thr Thr Val Thr Val Ser Ser 115 <210> 38 ' <211> 106 <212> PRT <213> Mus musculus <400> 38 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr 8.5 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 <210> 39 <211> 1039 <212> DNA <213> Homo sapiens <400> 39 60 tectgeaeag geagtgeett gaagtgette tteagagaee tttetteata gaetaetttt ttttctttaa gcagcaaaag gagaaaattg tcatcaaagg atattccaga ttcttgacag 120 cattetegte atetetgagg acateaceat cateteagga tgaggggcat gaagetgetg 180 240 qqqqcqctgc tggcactggc ggccctactg cagggggccg tgtccctgaa gatcgcagcc 300 ttcaacatcc agacatttgg ggagaccaag atgtccaatg ccaccctcgt cagctacatt gtgcagatcc tgagccgcta tgacatcgcc ctggtccagg aggtcagaga cagccacctg 360 420 actgoogtgg ggaagctgct ggacaacctc aatcaggatg caccagacac ctatcactac

gtggtcagtg agccactggg acggaacagc tataaggagc gctacctgtt cgtgtacagg

43

cctqaccaqq tqtctqcqqt qqacaqctac tactacqatq atgqctqcqa qccctqcqqq 540 aacqacacct tcaaccqaqa qccaqccatt qtcaqqttct tctcccggtt cacagaggtc, 600 agggagttig ccattgtice cetgeatgeg geeeggggg acgeagtage egagategae 660 gctctctatg acgtctacct ggatgtccaa gagaaatggg gcttggagga cgtcatgttg 720 780 atgggcgact tcaatgcggg ctgcagctat gtgagaccct cccagtggtc atccatccgc ctgtggacaa gccccacctt ccagtggctg atccccgaca gcgctgacac cacagctaca 840 cccacgcact gtgcctatga caggatcgtg gttgcaggga tgctgctccg aggcgccgtt 900 960 qttcccqact cqqctcttcc ctttaacttc caqqctqcct atgqcctgag tgaccaactg geccaageca teagtgacea etatecagtg gaggtgatge tgaagtgage ageceeteee 1020 1039 cacaccagtt gaactgcag

<210> 40

<211> 282

<212> PRT

<213> Homo sapiens

<400> 40

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Leu 1 10 15

Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr 20 25 30

Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val 35 40 45

Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp 50 55 60

Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp 65 70 75 80

Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn 85 90 95

Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser 100 105 110

Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn 115 120 125

Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe 130 135 140

Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly 145 150 155 160

Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val 165 170 175

Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn 180 185

Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu 195 Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr 215 Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn 250 245 Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser 265 Asp His Tyr Pro Val Glu Val Met Leu Lys 280 <210> 41 <211> 678 <212> DNA <213> Mus musculus <400> 41 gacatettge tgacteagte tecagecate etgtetgtga gtecaggaga aagagteagt 60 tteteetgea gggeeagtea gttegttgge teaageatee actggtatea geaaagaaca 120 aatggttctc caaaggcttct cataaagtat gcttctgagt ctatgtctgg gatcccttcc 180 240 aggtttagtg gcagtggatc agggacagat tttactctta gcatcaacac tgtggagtct 300 qaaqatattq cagattatta ctgtcaacaa agtcatagct ggccattcac gttcggctcg 360 qqqacaaatt tqqaaqtaaa agaaqtgaag cttgaggagt ctggaggagg cttggtgcaa cctqqaqqat ccatqaaact ctcctqtqtt gcctctggat tcattttcag taaccactgg 420 480 atqaactqqq toogocagto tocagagaag gggcttgagt gggttgctga aattagatca 540 aaatctatta attctgcaac acattatgcg gagtctgtga aagggaggtt caccatctca agagatgatt ccaaaagtgc tgtctacctg caaatgaccg acttaagaac tgaagacact 600 660 qqcqtttatt actgttccag gaattactac ggtagtacct acgactactg gggccaaggc 678 accactetca cagtetee <210> 42 <211> 226 <212> PRT <213> Mus musculus <400> 42 Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser 20 25 30

Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser 75 70 Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu 105 Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val 135 Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser 145 150 Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg 165 Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met 180 Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn 200 Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr 210 215 Val Ser 225 <210> 43 <211> 450 <212> DNA <213> Homo sapiens <400> 43 getgeateag aagaggeeat caageacate actgteette tgeeatggee etgtggatge 60 120 gcctcctgcc cctgctggcg ctgctggccc tctggggacc tgacccagcc gcagcctttg tgaaccaaca cctgtgcggc tcacacctgg tggaagctct ctacctagtg tgcggggaac 180 qaqqcttctt ctacacaccc aagacccgcc gggaggcaga ggacctgcag gtggggcagg 240 tggagctggg cgggggccct ggtgcaggca gcctgcagcc cttggccctg gaggggtccc 300 tgcagaagcg tggcattgtg gaacaatgct gtaccagcat ctgctccctc taccagctgg 360 agaactactg caactagacg cagecegeag geageeeece accegeegee teetgeaceg 420 450 agagagatgg aataaagccc ttgaaccagc

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47

720

780

840

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<210> 46

<211> 400

<212> PRT

<213> Hepatitis B virus

<400> 46

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro 20 25 30

Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn 35 40 45

Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly 50 55 60

Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln 65 70 75 80

Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser 85 90 95

Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu 100 105 110

Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His 115 120 125 .

Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly 130 135 140

Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro 145 150 155 160

Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu 165 170 175

Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly 180 185 190

Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser 195 200 205

Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly 210 215 220

| Gln 225 | Asn | Ser | Gln | Ser | Pro 230 | Thr | Ser | Asn | His | Ser 235 | Pro | Thr | Ser | Cys | Pro 240 | |
|------------------------------|------------|--------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----|
| Pro | Ile | Cys | Pro | Gly 245 | Tyr | Arg | Trp | Met | Cys 250 | Leu | Arg | Arg | Phe | Ile 255 | Ile | |
| Phe | Leu | Phe | Ile 260 | Leu | Leu | Leu | Суз | Leu 265 | Ile | Phe | Leu | Leu | Val 270 | Leu | Leu | |
| Asp | Tyr | Gln 275 | Gly | Met | Leu | Pro | Val 280 | Cys | Pro | Leu | Leu | Pro 285 | Gly | Thr | Ser | |
| Thr | Thr 290 | Ser | Thr | Gly | Pro | Cys 295 | Lys | Thr | Суз | Thr | Ile 300 | Pro | Ala | Gln | Gly | |
| Thr 305 | Ser | Met | Phe | Pro | Ser 310 | Cys | Cys | Суз | Thr | Lys 315 | Pro | Ser | Asp | Gly | Asn 320 | , |
| Суз | Thr | Суз | Ile | Pro 325 | Ile | Pro | Ser | Ser | Trp 330 | Ala | Phe | Ala | Arg | Phe 335 | Leu | |
| Trp | Glu | Trp | Ala 340 | Ser | Val | Arg | Phe | Ser 345 | Trp | Leu | Ser | Leu | Leu 350 | Val | Pro | |
| Phe | Val | Gln 355 | Trp | Phe | Ala | Gly | Leu 360 | Ser | Pro | Thr | Val | Trp 365 | Leu | Ser | Val | |
| Ile | Trp 370 | Met | Met | Trp | Tyr | Trp 375 | Gʻly | Pro | Ser | Leu | Tyr 380 | Asn | Ile | Leu | Ser | |
| Pro 385 | Phe | Leu | Pro | Leu | Leu 390 | Pro | Ile | Phe | Phe | Суs 395 | Leu | Trp | Val | Tyr | Ile 400 | |
| <210 <211 <212 <213 | l> ' | 47 799 DNA Homo | sapi | iens | | | | | | | | | | | | |
| <400 cgaa | | 47 ctc a | agggt | teet | gt gg | gacaç | gata | a cct | caget | tgca | atg | gctad | cag | gctco | ccggac | 60 |
| gtco | cctg | ctc · | ctgg | cttt | tg go | cctgo | ctctç | g act | gcc | ctgg | ctto | caaga | agg (| gcagt | gcctt | 120 |
| ccca | acca | att (| ccctt | tatc | ca go | gaatt | tttga | a caa | acgct | tatg | ctc | cgcgo | ccc . | atcgt | ctgca | 180 |
| ccaç | gatg | gee : | tttga | acac | ct ac | ccag | gagtt | tga | aagaa | agcc | tata | atcc | caa . | aggaa | acagaa | 240 |
| gtat | tcat | ttc · | ctgca | agaa | cc c | ccaga | accto | c cct | ctgt | tttc | tcaç | gagto | cta | ttcc | gacacc | 300 |
| ctc | caaca | agg (| gagga | aaac | ac aa | acaga | aaato | c caa | accta | agag | ctg | ctcc | gca | tctc | cctgct | 360 |
| gcto | catco | cag | tcgt | ggct | gg aq | gaaaq | gtgca | a gti | ccct | cagg | agto | gtcti | tcg | ccaa | cagcct | 420 |
| ggt | gtac | ggc (| gccto | ctga | ca go | caac | gtcta | a tga | accto | ccta | aagg | gacct | tag . | aggaa | aggcat | 480 |
| ccaa | aacgo | ctg . | atgg | ggag | ga to | ggaaq | gatgo | g caq | gece | ccgg | acto | gggca | aga | tctt | caagca | 540 |
| gaco | ctaca | agc . | aagti | tcga | ca ca | aaact | tcaca | a caa | acgat | tgac | gcad | ctact | tca | agaad | ctacgg | 600 |
| gct | gata | tac ' | tgcti | tcag | ga aq | ggac | atgga | a caa | aggto | cgag | acat | tcct | tgc | gcato | cgtgca | 660 |

780

799

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<400> 49

<213> Homo sapiens

PCT/US2003/031974 WO 2004/033651

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| gtcccggccg | agtgcttcga | cctgctggtc | cgccactgcg | tggcctgcgg | gctcctgcgc | 180 |
| acgccgcggc | cgaaaccggc | cggggccagc | agccctgcgc | ccaggacggc | gctgcagccg | 240 |
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| ccgtgcccag | cacctgaact | cctgggggga | ccgtcagtct | tectettece | cccaaaaccc | 360 |
| aaggacaccc | tcatgatctc | ccggacccct | gaggtcacat | gcgtggtggt | ggacg‡gagc | 420 |
| cacgaagacc | ctgaggtcaa | gttcaactgg | tacgtggacg | gcgtggaggt | gcataatgcc | 480 |
| aagacaaagc | cgcgggagga | gcagtacaac | agcacgtacc | gtgtggtcag | cgtcctcacc | 540 |
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| ctcccagccc | ccatcgagaa | aaccatctcc | aaagccaaag | ggcagccccg | agaaccacag | 660 |
| gtgtacaccc | tgcccccatc | ccgggatgag | ctgaccaaga | accaggtcag | cctgacctgc | 720 |
| ctggtcaaag | gcttctatcc | cagcgacatc | gccgtggagt | gggagagcaa | tgggcagccg | 780 |
| gagaacaact | acaagaccac | gcctcccgtg | ttggactccg | acggeteett | cttcctctac | 840 |
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Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg 20 25

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Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro

Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro

Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr 90

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 100 105 110

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 120 Thr Pro Glu Val Thr Cys Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 155 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 185 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 195 200 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 215 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys 230 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 310 315 <210> 51 <211> 107 <212> PRT <213> Homo sapiens <400> 51 Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly 10 Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 40 · 45 Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro 70 75

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Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys 100

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Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 70

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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<213> Homo sapiens

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Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 55

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 70

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys 85

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly 105

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Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr

Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr

Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly

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Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 55

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro 70

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala 105

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

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Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

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Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 55 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
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Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly 100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro

205 195 200 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys 215 Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 250 Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 310 Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 330 325 Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 345 Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr 360 355 Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 375 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 395 385 390 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys 410 405 Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu 425 430 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly 440 <210> 57 <211> 8540 <212> DNA <213> Homo sapiens <400> 57 gacgtcgcgg ccgctctagg cctccaaaaa agcctcctca ctacttctgg aatagctcag

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| <210 <211 <212 <213 | L> 2> | 61 420 DNA Mus | muscı | ulus | | | | | | | | | | | | |
| <400 atgg | | 61 gga | gcct | catc | tt go | ctcti | ccti | t gto | eget | gttg | ctad | cgcgt | tgt (| cctgi | cccag | 60 |
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| tgca | aagg | ctt | ctgg | ctac | ac at | tttad | ccag | t ta | caat | atgc | acto | gggta | aaa . | acaga | acacct | 180 |
| | | | | | | | | | | | | | | | acaat | |
| caga | aagt | tca | aagg | caag | ga a | acati | tgac | t gca | agac | aaat | cct | ccago | cac . | agcct | tacatg | 300 |
| cago | ctca | .gca | gcct | gaca | tc to | gagga | actc | t gc | ggtc | tatt | act | gtgca | aag | atcga | acttac | 360 |
| tac | ggcg | gtg | actg | gtac | tt c | aatgi | tctg | g gg(| cgca | ggga | cca | cggt | cac | cgtc | tctgca | 420 |
| <210 <210 <210 <210 | 1> 2> | 62 140 PRT Mus | musc | ulus | | | | | | | | | | | | |
| <400 Met 1 | | 62 Trp | Ser | Leu 5 | Ile | Leu | Leu | Phe | Leu 10 | Val | Ala | Val | Ala | Thr 15 | Arg | |

Val Leu Ser Gl
n Val Gl
n Leu Gl
n Gl
n Pro Gly Ala Glu Leu Val Lys $20 \\ 25 \\ 30$

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$

Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu 50 60

Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Ser 90 95

Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val 100 105 110

Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn 115 120 125

Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala 130 135 140

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<211> 1395

<212> DNA

<213> Homo sapiens

<400> 63

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<211> 464

<212> PRT

<213> Homo sapiens

<400> 64

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Tyr Leu Leu Ser Leu Leu Leu Ile Gly Phe Trp Asp Cys Val Thr Cys 20 25 30

His Gly Ser Pro Val Asp Ile Cys Thr Ala Lys Pro Arg Asp Ile Pro 35 40 45

Met Asn Pro Met Cys Ile Tyr Arg Ser Pro Glu Lys Lys Ala Thr Glu 50 55 60

Asp Glu Gly Ser Glu Gln Lys Ile Pro Glu Ala Thr Asn Arg Arg Val 65 70 75 80

Trp Glu Leu Ser Lys Ala Asn Ser Arg Phe Ala Thr Thr Phe Tyr Gln 85 90 95

His Leu Ala Asp Ser Lys Asn Asp Asn Asp Asn Ile Phe Leu Ser Pro 100 105 110

Leu Ser Ile Ser Thr Ala Phe Ala Met Thr Lys Leu Gly Ala Cys Asn 115 120 125

Asp Thr Leu Gln Gln Leu Met Glu Val Phe Lys Phe Asp Thr Ile Ser 130 135 140

Glu Lys Thr Ser Asp Gln Ile His Phe Phe Phe Ala Lys Leu Asn Cys 145 150 155

Arg Leu Tyr Arg Lys Ala Asn Lys Ser Ser Lys Leu Val Ser Ala Asn 165 170 175

Arg Leu Phe Gly Asp Lys Ser Leu Thr Phe Asn Glu Thr Tyr Gln Asp 180 185

Ile Ser Glu Leu Val Tyr Gly Ala Lys Leu Gln Pro Leu Asp Phe Lys

200 205 195 Glu Asn Ala Glu Gln Ser Arg Ala Ala Ile Asn Lys Trp Val Ser Asn 215 Lys Thr Glu Gly Arg Ile Thr Asp Val Ile Pro Ser Glu Ala Ile Asn Glu Leu Thr Val Leu Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Leu 250 245 Trp Lys Ser Lys Phe Ser Pro Glu Asn Thr Arg Lys Glu Leu Phe Tyr Lys Ala Asp Gly Glu Ser Cys Ser Ala Ser Met Met Tyr Gln Glu Gly 280 Lys Phe Arg Tyr Arg Arg Val Ala Glu Gly Thr Gln Val Leu Glu Leu 295 Pro Phe Lys Gly Asp Asp Ile Thr Met Val Leu Ile Leu Pro Lys Pro 315 Glu Lys Ser Leu Ala Lys Val Glu Lys Glu Leu Thr Pro Glu Val Leu 330 Gln Glu Trp Leu Asp Glu Leu Glu Glu Met Met Leu Val Val His Met 345 Pro Arg Phe Arg Ile Glu Asp Gly Phe Ser Leu Lys Glu Gln Leu Gln 360 Asp Met Gly Leu Val Asp Leu Phe Ser Pro Glu Lys Ser Lys Leu Pro 375 Gly Ile Val Ala Glu Gly Arg Asp Asp Leu Tyr Val Ser Asp Ala Phe 395 390 385 His Lys Ala Phe Leu Glu Val Asn Glu Glu Gly Ser Glu Ala Ala Ala 410 405 Ser Thr Ala Val Val Ile Ala Gly Arg Ser Leu Asn Pro Asn Arg Val 425 Thr Phe Lys Ala Asn Arg Pro Phe Leu Val Phe Ile Arg Glu Val Pro 440 Leu Asn Thr Ile Ile Phe Met Gly Arg Val Ala Asn Pro Cys Val Lys 455 <210> 65 <211> 1962 <212> DNA <213> Homo sapiens <400> 65 atgegteece tgegeeceeg egeegegetg etggegetee tggeeteget eetggeegeg

70

18

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tggccctgc ggcgcttctg gaggagcaca ggcttctgcc ccccgctgcc acacagccag

| gctgaccagt acgtcctcag | ctgggaccag | cagctcaacc | tcgcctatgt | gggcgccgtc | 240 |
|-----------------------|--------------|------------|------------|------------|------|
| cctcaccgcg gcatcaagca | ggtccggacc | cactggctgc | tggagcttgt | caccaccagg | 300 |
| gggtccactg gacggggcct | gagctacaac | ttcacccacc | tggacgggta | cttggacctt | 360 |
| ctcagggaga accagctcct | cccagggttt | gagctgatgg | gcagcgcctc | gggccacttc | 420 |
| actgactttg aggacaagca | gcaggtgttt | gagtggaagg | acttggtctc | cagcctggcc | 480 |
| aggagataca tcggtaggta | cggactggcg | catgtttcca | agtggaactt | cgagacgtgg | 540 |
| aatgagccag accaccacga | ctttgacaac | gtctccatga | ccatgcaagg | cttcctgaac | 600 |
| tactacgatg cctgctcgga | gggtctgcgc | geegeeagee | ccgccctgcg | gctgggaggc | 660 |
| cccggcgact ccttccacac | cccaccgcga | tccccgctga | gctggggcct | cctgcgccac | 720 |
| tgccacgacg gtaccaactt | cttcactggg | gaggcgggcg | tgcggctgga | ctacatctcc | 780 |
| ctccacagga agggtgcgcg | cagctccatc | tccatcctgg | agcaggagaa | ggtcgtcgcg | 840 |
| cagcagatcc ggcagctctt | ccccaagttc | gcggacaccc | ccatttacaa | cgacgaggcg | 900 |
| gacccgctgg tgggctggtc | cctgccacag | ccgtggaggg | cggacgtgac | ctacgcggcc | 960 |
| atggtggtga aggtcatcgc | gcagcatcag | aacctgctac | tggccaacac | cacctccgcc | 1020 |
| ttcccctacg cgctcctgag | caacgacaat | gccttcctga | gctaccaccc | gcaccccttc | 1080 |
| gcgcagcgca cgctcaccgc | gcgcttccag | gtcaacaaca | cccgcccgcc | gcacgtgcag | 1140 |
| ctgttgcgca agccggtgct | cacggccatg | gggctgctgg | cgctgctgga | tgaggagcag | 1200 |
| ctctgggccg aagtgtcgca | ggccgggacc | gtcctggaca | gcaaccacac | ggtgggcgtc | 1260 |
| ctggccagcg cccaccgccc | ccagggcccg | gccgacgcct | ggcgcgccgc | ggtgctgatc | 1320 |
| tacgcgagcg acgacacccg | cgcccacccc | aaccgcagcg | tcgcggtgac | cctgcggctg | 1380 |
| cgcggggtgc ccccggccc | gggcctggtc | tacgtcacgc | gctacctgga | caacgggctc | 1440 |
| tgcagccccg acggcgagtg | geggegeetg | ggccggcccg | tcttccccac | ggcagagcag | 1500 |
| tteeggegea tgegegegge | tgaggacccg | gtggccgcgg | cgccccgccc | cttacccgcc | 1560 |
| ggeggeegee tgaeeetgeg | ccccgcgctg | cggctgccgt | cgcttttgct | ggtgcacgtg | 1620 |
| tgtgcgcgcc ccgagaagcc | gcccgggcag | gtcacgcggc | teegegeeet | gcccctgacc | 1680 |
| caagggcagc tggttctggt | ctggtcggat | gaacacgtgg | gctccaagtg | cctgtggaca | 1740 |
| tacgagatcc agttctctca | . ggacggtaag | gcgtacaccc | cggtcagcag | gaagccatcg | 1800 |
| accttcaacc tctttgtgtt | cageceagae | acaggtgctg | tetetggete | ctaccgagtt | 1860 |
| cgagccctgg actactgggc | cegaceagge | cccttctcgg | accctgtgcc | gtacctggag | 1920 |
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- <211> 653
- <212> PRT
- <213> Homo sapiens

<400> 66

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- Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val 20 25 30
- Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg 35 40 45
- Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr 50 60
- Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val 65 70 75 80
- Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu 85 90 95
- Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr 100 105 110
- His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro 115 120 125
- Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu 130 135 140
- Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala 145 150 155 160
- Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn 165 170 175
- Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser
- Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly 195 200 205
- Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser 210 215 220
- Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His 225 230 235 240
- Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu 245 250 255
- Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile 260 265 270
- Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro 275 280 285
- Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val

290 295 300

Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala 305 $310 \hspace{1.5cm} 315 \hspace{1.5cm} 320$

Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Ala Asn 325 330 335

Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe 340 345 350

Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg 355 360 365

Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys 370 375 380

Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln 385 390 395 400

Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His 405 410 415

Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp
420 425 430

His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro 450 455 460

Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu 465 470 475 480

Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro 485 490 495

Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala 500 505 510

Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro 515 520 525

Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro 530 535 540

Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr 545 550 555 560

Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys
565 570 575

Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr 580 585 590

Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser 595 600 605

Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp 610 620

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Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro 645 650

<210> 67

<211> 1290

<212> DNA

<213> Homo sapiens

<400> 67

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<210> 68

<211> 429

<212> PRT

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<400> 68

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Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu 20 25 30

Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu 35 40 45

Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile 50 55 60

Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly 65 70 75 80

Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met 85 90 95

Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg
100 105 110

Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly 115 120 125

Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly 130 135 140

Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala 145 150 155 160

Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser 165 170 175

Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn 180 185 190

Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met 195 200 205

Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn 210 215 220

His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys 225 230 235 240

Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val 245 250 255

Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn 260 265 270

Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gln Met Ala Leu Trp Ala 275 280 285

Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser 290 295 300

Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn 305 310 315 320

Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn 330 Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala 345 Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile 375 Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln 410 Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu <210> 69 <211> 351 <212> DNA <213> Homo sapiens <400> 69 atggattact acagaaaata tgcagctatc tttctggtca cattgtcggt gtttctgcat 60 gttctccatt ccgctcctga tgtgcaggat tgcccagaat gcacgctaca ggaaaaccca 120 ttettetece ageegggtge eccaataett eagtgeatgg getgetgett etetagagea 180 tateceacte cactaaggte caagaagaeg atgttggtee aaaagaaegt caceteagag 240 tocacttgct gtgtagctaa atcatataac agggtcacag taatgggggg tttcaaagtg 300 qagaaccaca cggcgtgcca ctgcagtact tgttattatc acaaatctta a 351 <210> 70 <211> 116 <212> PRT <213> Homo sapiens <400> 70 Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr 105 Tyr His Lys Ser 115 <210> 71 <211> 498 <212> DNA <213> Homo sapiens <400> 71 60 atqqaqatqt tocaqqqqot qotqotqttg otgotgotga gcatgggogg gacatgggca 120 tecaaqqaqe eqetteqqee aeqqtqeeqe eccateaatq ccaecetqqe tqtqqaqaaq 180 gagggctgcc ccgtgtgcat caccgtcaac accaccatct gtgccggcta ctgccccacc atgaccegeg tgctgcaggg ggtcctgccg gccctgcctc aggtggtgtg caactaccgc 240 300 gatgtgcgct tcgagtccat ccggctccct ggctgcccgc gcggcgtgaa ccccgtggtc tectaegeeg tggeteteag etgteaatgt geactetgee geegeageae caetgaetge 360 420 gggggtccca aggaccacco cttgacctgt gatgaccccc gcttccagga ctcctcttcc tcaaaggccc ctcccccag ccttccaagc ccatcccgac tcccggggcc ctcggacacc 480 ccgatcctcc cacaataa 498 <210> 72 <211> 165 <212> PRT <213> Homo sapiens <400> 72 Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Ser Met Gly 5 10 Gly Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr 35 40 45 Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg 70 75 Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu 105 110

Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu

115 120 125

Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro 130 135 140

Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr 145 150 155 160

Pro Ile Leu Pro Gln 165

<210> 73

<211> 165

<212> PRT

<213> Homo sapiens

<400> 73

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Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His 20 25 30

Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe 35 40 45

Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp 50 55 60

Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu 65 70 75 80

Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp 85 90 95

Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu 100 105 110

Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala 115 120 125

Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val 130 135 140

Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala 145 150 155 160

Cys Arg Thr Gly Asp 165

<210> 74

<211> 588

<212> DNA

<213> Homo sapiens

<400> 74

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ctgcaccaaa tgaggagaat ctcccctttc ttgtgtctca aggacagaag agacttcagg 180

PCT/US2003/031974 WO 2004/033651

| ttcccccagg agatggtaaa agggagccag ttgcagaagg cccatgtca | t gtctgtcctc 240 |
|--|--------------------|
| catgagatgc tgcagcagat cttcagcctc ttccacacag agcgctcct | c tgctgcctgg 300 |
| aacatgaccc tectagacca actecacact ggaetteate ageaactge | a acacctggag 360 |
| acctgcttgc tgcaggtagt gggagaagga gaatctgctg gggcaatta | g cagecetgea 420 |
| ctgaccttga ggaggtactt ccagggaatc cgtgtctacc tgaaagaga | a gaaatacagc 480 |
| gactgtgcct gggaagttgt cagaatggaa atcatgaaat ccttgttct | t atcaacaaac 540 |
| atgcaagaaa gactgagaag taaagataga gacctgggct catcttga | 588 |
| <210> 75 <211> 195 <212> PRT / <213> Homo sapiens | |
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| Ser Pro Val Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn F | His Gly Leu 80 |
| Leu Ser Arg Asn Thr Leu Val Leu Leu His Gln Met Arg F 35 40 45 | Arg Ile Ser |
| Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe Arg Phe E 50 55 60 | Pro Gln Glu |
| Met Val Lys Gly Ser Gln Leu Gln Lys Ala His Val Met 8 65 70 75 | Ser Val Leu 80 |
| His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His Thr C 85 90 | Glu Arg Ser 95 |
| Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His T | Thr Gly Leu 110 |
| His Gln Gln Leu Gln His Leu Glu Thr Cys Leu Leu Gln V 115 120 125 | Val Gly |
| Glu Gly Glu Ser Ala Gly Ala Ile Ser Ser Pro Ala Leu 130 135 140 | Thr Leu Arg |
| Arg Tyr Phe Gln Gly Ile Arg Val Tyr Leu Lys Glu Lys 1 145 150 155 | Lys Tyr Ser 160 |
| Asp Cys Ala Trp Glu Val Val Arg Met Glu Ile Met Lys : 165 170 | Ser Leu Phe 175 |
| Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser Lys Asp 180 | Arg Asp Leu 190 |
| Gly Ser Ser 195 | |